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               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
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=> file medicine
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=> s deoxyuridine
L1       56898 DEOXYURIDINE

=> s l1 and rheumatoid arthritis
  31 FILES SEARCHED...
L2         335 L1 AND RHEUMATOID ARTHRITIS

=> s l2 and pd<2001
   4 FILES SEARCHED...
'2001' NOT A VALID FIELD CODE
   9 FILES SEARCHED...
'2001' NOT A VALID FIELD CODE
'2001' NOT A VALID FIELD CODE
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  32 FILES SEARCHED...
  33 FILES SEARCHED...
L3         120 L2 AND PD<2001

=> s l3 and phosphoryl
L4           1 L3 AND PHOSPHORYL

=> d l4 1

L4   ANSWER 1 OF 1  USPATFULL
AN     88:69159  USPATFULL
TI     F-substituted-3-.beta.-D-ribofuranosyl-3H-imidazo[4,5-b]pyridines and
       pharmaceutical compositions thereof
```

IN Krenitsky, Thomas A., Chapel Hill, NC, United States
Rideout, Janet L., Raleigh, NC, United States
Koszalka, George W., Apex, NC, United States
PA Burroughs Wellcome Co., Research Triangle Park, NC, United States (U.S. corporation)
PI US 4780452 19881025 <--
AI US 1986-905243 19860908 (6)
DT Utility
FS Granted
LN.CNT 780
INCL INCLM: 514/045.000
INCLS: 514/046.000; 514/049.000; 514/050.000; 536/023.000; 536/024.000; 536/026.000
NCL NCLM: 514/045.000
NCLS: 514/046.000; 514/049.000; 514/050.000; 536/027.140; 536/027.200
IC [4]
ICM: A61K031-70
ICS: C07H017-02
EXF 514/42; 514/45; 536/24; 536/28
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d l4 1 kwic

L4 ANSWER 1 OF 1 USPATFULL
PI US 4780452 19881025 <--
SUMM . . . pain following general dental procedures, oral and general surgery, dysmenorrhea, myalgia, pain of unresectable cancer, joint and peripheral nerve disorders, **rheumatoid arthritis**, rheumatoid spondylitis, osteoarthritis, gouty arthritis and other arthritic conditions, pyresis and other conditions associated with pain, inflammation and fever. They. . .
SUMM . . . position by phosphorylation using traditional phosphorylating agents such as trialkyl phosphates, e.g., triethyl phosphate, with a phosphorus oxyhalide such as **phosphoryl** chloride. When this technique is used it is advantageous to block the 2'- and 3'-positions of the ribose moiety either. . .
SUMM Rather than block the 2'- and 3'-positions as described above, it is preferred to use **phosphoryl** chloride in the presence of a trialkylphosphate (preferably triethyl phosphate) and a trace of water at a temperature of about. . .
DETD 7-Anilino-3H-imidazo[4,5-b]pyridine (0.8 g, 3.7 mmol) and 5'-chloro-5'-**deoxyuridine** (15 g, 5.7 mmol) were combined in 10 mL of 10 mM K.sub.x H.sub.x PO.sub.4, pH 7.4. Uridine phosphorylase (315. . .
DETD 7-Anilino-3H-imidazo[4,5-b]pyridine (0.8 g, 3.77 mmol) and 5'-**deoxyuridine** (2 g, 0.87 mmol) were added to a 10 mL solution of 10 mM K.sub.x H.sub.x PO.sub.4, pH 7.4 and. . .

=> s l1 and phosphoramidatyl
L5 4 L1 AND PHOSPHORAMIDATYL

=> d l5 1-4

L5 ANSWER 1 OF 4 IFIPAT COPYRIGHT 2003 IFI
AN 10365280 IFIPAT;IFIUDB;IFICDB
TI NOVEL PHOSPHORAMIDATE COMPOUNDS AND METHODS OF USE
IN Lehsten Danielle M; Shepard H Michael; Vaino Andrew Rein
PA Unassigned Or Assigned To Individual (68000)
PI US 2003109697 A1 20030612
AI US 2002-119927 20020409
RLI US 1999-235961 19990122 CONTINUATION 6339151

US 2001-782721 20010212 CONTINUATION-IN-PART
PRAI US 1998-72264P 19980123 (Provisional)
US 1998-76950P 19980305 (Provisional)
US 1998-108634P 19981116 (Provisional)
FI US 2003109697 20030612
US 6339151
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 30
GI 9 Figure(s).

FIG. 1 is a graph showing fluorescent products from incubation of Bromovinyl, 2'-**Deoxyuridine** Monophosphate ("BVdUMP") with Recombinant Human Thymidylate Synthase ("rHuTS"). Incubation of BVdUMP with thymidylate synthase ("TS") results in a time and enzyme dependent generation of fluorescent product(s). BVdUMP was incubated with the indicated amounts of rHuTS in the standard reaction mixture at 30 degrees C. (Materials and Methods), except that N5, N10-methylenetetrahydrofolate was omitted from the reaction. The numbers adjacent to each data curve refer to TS enzyme units.

FIG. 2 shows the results of an experiment that demonstrates that preincubation with BVdUMP does not inactivate rHuTS. Human thymidylate synthase was pre-incubated in reaction mixtures with and without 125 mu M BVdUMP. After 20 hours, BVdUMP was added to a concentration of 125 mu M, dUMP to a final concentration of 125 mu M, and N5, N10-methylene tetrahydrofolate was added to 70 mu M. Thymidylate synthase activity was determined by measuring the increase in A340. Solid circles (preincubated reaction), Open circles (no preincubation).

FIGS. 3A and 3B show detection of BVdUMP in H630R10 cells treated with NB1011. H630 R10 cells were treated with 100 mu M NB1011 for 5 days, then analyzed by LC/MS as described in Materials and Methods.

FIG. 4 demonstrates that NB1011 does not irreversibly inactivate TS in vivo. The effect of NB1011 on TS activity in intact cells is completely reversible. TS activity was measured in intact RKO cells by release of (3H)2O from 5-(3H)**deoxyuridine** as described in Materials and Methods. NB1011 was washed out of cells by replacing with fresh media, incubating for 60 minutes at 37 degrees C., then repeating this procedure. Control and untreated cells were subjected to the same washing procedure.

FIGS. 5A and 5B show that there are marked similarities between in vitro efficacy requirements for NB1011 and anti-HER2. A), Data are taken from Tables 4, 5, and 8. B). Data from Shepard, et al. (1991). Vertical bars show standard error of means calculated using the Mann-Whitney U test.

FIG. 6 shows that NB1011 is highly active against Tomudex resistant cancers. Cytotoxicity vs. TDXR cell lines was measured in the alamarBlue assay, as described in Materials and Methods, below.

FIG. 7 shows transcript levels of thymidylate synthase in human normal and tumor colon tissues. RT-PCR analysis was performed as described in Materials and Methods, below. The ratio of TS mRNA in tumor vs. normal tissue samples, each normalized to beta-actin was (left to right) 14.35, 7.31, 0.75, 59.5, 2.53, 24.1, and 4.0.

FIG. 8A shows that NB1011 inhibits growth of 5-FU resistant colon cancer. Treatment of nude mice bearing H630R10 (5FU Resistant) human colon carcinoma. Tumor measurements began on the first day of treatment (Day 1).

FIG. 8B shows long term response to NB1011. Analysis of pooled data at Day 25. Statistical analysis is described in the Materials and Methods section below.

L5 ANSWER 2 OF 4 IFIPAT COPYRIGHT 2003 IFI
AN 10207812 IFIPAT;IFIUDB;IFICDB
TI METHODS TO TREAT AUTOIMMUNE AND INFLAMMATORY CONDITIONS

IN Shepard H Michael
PA Unassigned Or Assigned To Individual (68000)
PI US 2002151519 A1 20021017
AI US 2002-51320 20020118
PRAI US 2001-262849P 20010119 (Provisional)
FI US 2002151519 20021017
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 22
GI 3 Figure(s).
FIG. 1 shows clinical scoring of animals with collagen-induced arthritis using NB 1011, a 5'-**phosphoramidatyl deoxyuridine** derivate and controls.
FIG. 2 shows therapeutic effect on paw swelling in animals with collagen-induced arthritis.
FIG. 3 shows histological evaluation of all joints performed by an observer blinded to the treatments received. This figure represents the percentage of joints exhibiting normal, mild or moderate to severe arthritic changes in the joint architecture in different treatment groups. Chi-square test (2 x 2 correlation) was done to calculate statistical significance of data. P less-than 0.05 (*) was considered significant.

L5 ANSWER 3 OF 4 USPATFULL
AN 2003:160082 USPATFULL
TI Novel phosphoramidate compounds and methods of use
IN Shepard, H. Michael, Encinitas, CA, UNITED STATES
Vaino, Andrew Rein, San Diego, CA, UNITED STATES
Lehsten, Danielle M., San Diego, CA, UNITED STATES
PI US 2003109697 A1 20030612
AI US 2002-119927 A1 20020409 (10)
RLI Continuation-in-part of Ser. No. US 2001-782721, filed on 12 Feb 2001, PENDING Continuation of Ser. No. US 1999-235961, filed on 22 Jan 1999, GRANTED, Pat. No. US 6339151
PRAI US 1998-72264P 19980123 (60)
US 1998-76950P 19980305 (60)
US 1998-108634P 19981116 (60)
DT Utility
FS APPLICATION
LN.CNT 3503
INCL INCLM: 536/026.800
INCLS: 514/051.000
NCL NCLM: 536/026.800
NCLS: 514/051.000
IC [7]
ICM: C07H019-048
ICS: C07H019-10; A61K031-7072
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 4 OF 4 USPATFULL
AN 2002:273391 USPATFULL
TI Methods to treat autoimmune and inflammatory conditions
IN Shepard, H. Michael, Encinitas, CA, UNITED STATES
PI US 2002151519 A1 20021017
AI US 2002-51320 A1 20020118 (10)
PRAI US 2001-262849P 20010119 (60)
DT Utility
FS APPLICATION
LN.CNT 1850
INCL INCLM: 514/050.000
INCLS: 514/051.000; 514/086.000

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NCL    NCLM:  514/050.000
       NCLS:  514/051.000; 514/086.000
IC     [7]
       ICM: A61K031-711
       ICS: A61K031-675
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> s d his
  28 FILES SEARCHED...
L6        1644 D HIS

=> d his

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     FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT,
     CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL,
     EMBASE, ESBIOBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF,
     MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ...' ENTERED AT 11:41:58 ON 08 JUL
     2003
L1        56898 S DEOXYURIDINE
L2          335 S L1 AND RHEUMATOID ARTHRITIS
L3          120 S L2 AND PD<2001
L4            1 S L3 AND PHOSPHORYL
L5            4 S L1 AND PHOSPHORAMIDATYL
L6         1644 S D HIS

=> s l2 and phosphoramidatyl
L7            3 L2 AND PHOSPHORAMIDATYL

=> d l3 bib, kwic

L3   ANSWER 1 OF 120  ADISNEWS COPYRIGHT (C) 2003 Adis Data Information BV
AN   1988:2445  ADISNEWS  ED  8 Aug 2001  UP  8 Aug 2001
DN   01149954-800503719
TI   ADR news: Agents provoking adverse gastrointestinal reactions.
SO   REACTIONS  14 Dec 1988  ISSN: 0114-9954
DT   (MIX)
WC   388
SO   REACTIONS  14 Dec 1988  ISSN: 0114-9954
TX.  .  .  aspirin injury is the same for old and young patients. Some evidence
     suggests a higher incidence of gastric ulceration in rheumatoid
     arthritis. In other areas of the gastrointestinal tract, a 2-fold
     increase in risk has been observed for intestinal perforation with NSAIDs.
     .  .  adverse effects occur in the gastrointestinal tract Fluorouracil can
     cause oral as well as esophageal and gastric ulceration and '5-fluoro-2-
     deoxyuridine' is associated with diarrhea with abdominal
     distension, fever and hypotension.
     In conclusion, 'the physician must remain vigilant for adverse reactions
     on.  .  .


=> d l7 1-3 1-3 bib, kwic

L7   ANSWER 1 OF 3  IFIPAT  COPYRIGHT 2003 IFI
AN    10207812  IFIPAT;IFIUDB;IFICDB
TI    METHODS TO TREAT AUTOIMMUNE AND INFLAMMATORY CONDITIONS
INF   Shepard; H. Michael, Encinitas, CA, US
IN    Shepard H Michael
PAF   Unassigned
PA    Unassigned Or Assigned To Individual (68000)
```

AG McCutchen, Doyle, Brown & Enersen LLP, Suite 1800, Three Embarcadero Center, San Francisco, CA, 94111, US
PI US 2002151519 A1 20021017
AI US 2002-51320 20020118
PRAI US 2001-262849P 20010119 (Provisional)
FI US 2002151519 20021017
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 22
GI 3 Figure(s).
FIG. 1 shows clinical scoring of animals with collagen-induced arthritis using NB 1011, a 5'-**phosphoramidatyl deoxyuridine** derivate and controls.
FIG. 2 shows therapeutic effect on paw swelling in animals with collagen-induced arthritis.
FIG. 3 shows histological evaluation of all joints performed by an observer blinded to the treatments received. This figure represents the percentage of joints exhibiting normal, mild or moderate to severe arthritic changes in the joint architecture in different treatment groups. Chi-square test (2 x 2 correlation) was done to calculate statistical significance of data. P less-than 0.05 (*) was considered significant.
AB . . . the affected cell or tissue with a therapeutic compound as described herein. Such pathologies include, but are not limited to **rheumatoid arthritis**, systemic lupus erythmatosus, psoriatic arthritis, reactive arthritis, Crohn's disease, ulcerative colitis and scleroderma. Therapeutic compounds useful in the methods of. . .
GI 3 Figure(s).
FIG. 1 shows clinical scoring of animals with collagen-induced arthritis using NB 1011, a 5'-**phosphoramidatyl deoxyuridine** derivate and controls.
FIG. 2 shows therapeutic effect on paw swelling in animals with collagen-induced arthritis.
FIG. 3 shows histological evaluation of. . .
ACLM 2. The method of claim 1, wherein the compound is a 1,5-substituted **deoxyuridine** derivative or analog.
4. The method of claim 2, wherein the 1,5-substituted **deoxyuridine** derivative or analog is a compound selected from the group consisting of a 5'-**phosphoramidatyl deoxyuridine**, a substituted 5'-phosphoramidyl **deoxyuridine**, a 5'-phosphoryl **deoxyuridine**, and a substituted, 5'-phosphoryl **deoxyuridine**.
5. The method of claim 2, wherein the 1,5-substituted **deoxyuridine** is substituted at the 5 position with a substituent selected from the group consisting of alkyl, alkenyl, alkynyl, vinyl, propargyl. . .
7. The method of claim 6, wherein the halogen-substituted derivative is a 5-haloalkyl substituted **deoxyuridine**.
8. The method of claim 7, wherein the compound is 5-bromovinyl substituted **deoxyuridine**.
9. The method of claim 4, wherein the 1,5-substituted **deoxyuridine** is a 5'-phosphoryl derivative of pyrimidine.
10. The method of claim 4, wherein the 1,5-substituted **deoxyuridine** is a 5'-**phosphoramidatyl** derivative of pyrimidine.
11. The method of claim 10, wherein the a 5'-**phosphoramidatyl** derivative is (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate.
. . . wherein the autoimmune disease is selected from the group consisting of multiple sclerosis, Type 1 diabetes, glomerulonephotis systemic lupus

erythematosus, **rheumatoid arthritis**, psoriatic arthritis, reactive arthritis, Sjogren's syndrome, graft-versus-host disease (GVHD), muscular dystrophy, myasthenia gravis, atherosclerosis and osteoarthritis.

. . . sample comprising suitable cells or tissue with an effective amount of a compound selected from the group consisting of a **deoxyuridine**, a substituted **deoxyuridine**, a substituted **deoxyuridine** derivative and analogs thereof and contacting a second sample of the suitable cells or tissue with the agent to be. . . 22. The assay of claim 21, wherein the substituted **deoxyuridine** derivative is (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate.

L7 ANSWER 2 OF 3 USPATFULL
AN 2003:160082 USPATFULL
TI Novel phosphoramidate compounds and methods of use
IN Shepard, H. Michael, Encinitas, CA, UNITED STATES
Vaino, Andrew Rein, San Diego, CA, UNITED STATES
Lehsten, Danielle M., San Diego, CA, UNITED STATES
PI US 2003109697 A1 20030612
AI US 2002-119927 A1 20020409 (10)
RLI Continuation-in-part of Ser. No. US 2001-782721, filed on 12 Feb 2001, PENDING Continuation of Ser. No. US 1999-235961, filed on 22 Jan 1999, GRANTED, Pat. No. US 6339151
PRAI US 1998-72264P 19980123 (60)
US 1998-76950P 19980305 (60)
US 1998-108634P 19981116 (60)
DT Utility
FS APPLICATION
LREP McCutchen, Doyle, Brown & Enersen LLP, Suite 1800, Three Embarcadero Center, San Francisco, CA, 94111
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 10 Drawing Page(s)
LN.CNT 3503
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB . . . cancer, infectious disease, an autoimmune disorder or an inflammatory condition. Therapeutic compounds useful in the methods of this invention are 5'-**phosphoramidatyl**, 1,5-substituted pyrimidine compounds, derivatives, analogs and pharmaceutically acceptable salts thereof
SUMM . . . (Cordan-Cardo, C. and Prives, C. (1999)) and/or defective apoptosis (programmed cell death) (Mountz, J. D. et al. (1994)). These include: **rheumatoid arthritis**, systemic lupus erythmatosus, psoriatic arthritis, reactive arthritis, Crohn's disease, ulcerative colitis and scleroderma. Table 1 lists literature examples which suggest. . . Tumor Suppressor Mutation/Inactivation Relates to Noncancer Hyperproliferative Disease, Autoimmune Disease and Inflammation.

Impact	Disease Effect	Reference
Increased IL6 (1999)	Proliferation	Han, et al.
	Inflammation **Rheumatoid Arthritis**	
Increased metalloproteinases (2000)	Tissue Degradation	Sun, Y. et al.
Increased proliferation of Aupperle, K. R. et al. synovial cells	**Rheumatoid arthritis**	(1998)
Genetic instability	Chronic inflammation	Tak, P. P. et

al.

(2000)

and disease progression Ulcerative colitis. . .

SUMM [0013] Novel **phosphoramidatyl**, 1,5-substituted pyrimidine compounds, derivatives, analogs, and pharmaceutically acceptable salts thereof and compositions containing the compounds are provided by this invention.. . .

SUMM . . . or an inflammatory condition, by delivering to the subject an effective amount of at least one or more of the 5'-**phosphoramidatyl**, 1,5-substituted pyrimidine, derivative, analog or pharmaceutically acceptable salt thereof. Methods for synthesizing the compounds are described herein and in Applicants'. . .

DRWD [0020] FIG. 1 is a graph showing fluorescent products from incubation of Bromovinyl, 2'-**Deoxyuridine** Monophosphate ("BVdUMP") with Recombinant Human Thymidylate Synthase ("rHuTS"). Incubation of BVdUMP with thymidylate synthase ("TS") results in a time and. . .

DRWD . . . activity in intact cells is completely reversible. TS activity was measured in intact RKO cells by release of [.sup.3H].sub.2O from 5-[.sup.3H]**deoxyuridine** as described in Materials and Methods. NB1011 was washed out of cells by replacing with fresh media, incubating for 60. . .

DRWD . . . produces antibodies or immune cells which recognize the organism's own molecules, cells or tissues. Non-limiting examples of autoimmune disorders include **rheumatoid arthritis**, Sjogren's syndrome, graft versus host disease, myasthenia gravis, and systemic lupus erythematosus.

DRWD . . . inflammatory diseases include Crohn's disease, psoriasis, and asthma, are also included within the term "inflammatory condition." Autoimmune diseases such as **rheumatoid arthritis** and systemic lupus erythematosus can also result in a chronic inflammatory state.

DRWD [0080] Therapeutic compounds for use in the methods of this invention are one or more 5'-**phosphoramidatyl** 1,5-substituted pyrimidines, derivatives, analogs or pharmaceutically acceptable salts thereof. The compounds of this invention are nucleoside analogs comprising a substituted. . .

DRWD [0210] One method requires treatment of 5-chloromercuri-2'-**deoxyuridine** with haloalkyl compounds, haloacetates or haloalkenes in the presence of Li.sub.2PdCl.sub.4 to form, through an organopalladium intermediate, the 5-alkyl, 5-acetyl. . .

DRWD . . . monophosphate, 5' phosphodiester, or 5' protected ("masked") deoxyuridines or comparable derivatives of alternative carbohydrate moieties, as described below. Protected 5-substituted **deoxyuridine** monophosphate derivatives are those in which the phosphate moiety has been blocked through the attachment of suitable chemical protecting groups.. . .

DRWD [0220] Closely following the literature procedures, a t-butyldimethylsilyl propargyl ether-equipped 3', 5'-di-O-protected 2'-**deoxyuridine** (Graham, D. et al. (1998), and De Clercq, E. et al. (1983)) can be prepared and a portion of it,. . .

DRWD [0223] Synthesis of furano-pyrimidinones begins with synthesis of a C5 propargylic--alcohol-equipped 2'-**deoxyuridine**. Furano-pyrimidinone compounds are then be formed from the O-tetrahydropyranyl ether derivative described above. Synthesis proceeds by reaction of the second. . .

DRWD [0224] Furo[2,3-d]pyrimidinone nucleosides (represented by the above generic structure) were prepared by condensing 2',3'-di-O-p-toluoyl or 2',3'-di-O-acetyl-5-iodo-2'-**deoxyuridine** with 1-(tetrahydropyranyloxy)-2-propyne (Jones, R. G. and Mann, M. J. (1953)) under conditions known to promote the formation of these fluorescent. . .

DRWD . . . leaving groups to either the C6 fluoro-uridine base or the C4

hydrazone modified pyrimidine. Methods described above for synthesis of 2-**deoxyuridine** based compounds can again be employed for the synthesis of such molecules.

DETD [0243] The 4-nitrophenyl ether derivative of 5-(3-hydroxy-1-propynyl)-2'-**deoxyuridine** was prepared according to standard ether synthesis as shown below. ##STR42##

DETD 5-[3-(4-Nitrophenoxy)-1-propynyl]-2'-**deoxyuridine**

DETD [0244] A solution of pre-dried 5-(3-hydroxy-1 -propynyl)-2'-**deoxyuridine** (Robins, M. J. et al. (1983)) (565 mg, 2 mmol) in 40 mL of anhydrous THF under argon was treated. . .

DETD [0245] (a) 5-(Carbomethoxyvinyl)-2'-**deoxyuridine** -3',5'-bis(tetrahydro-2H-pyran-2-yl)ether (I)

DETD [0246] A slurry of 5-(carbomethoxyvinyl)-2'-**deoxyuridine** (3.0 g, 9.6 mmol), 3,4-dihydro-2H-pyran (22 mL, 21.3 mmol) and pyridinium p-toluenesulfonate (PPTS, 0.242 g, 0.96 mmol) in dimethylformamide (DMF,. . .

DETD [0247] (b) 5-(3-Hydroxyprop-1-enyl)-2'-**deoxyuridine**-3 ',5'-bis(tetrahydro-2H-pyran-2-yl)ether (II)

DETD . . . mmol) were added and the solution was heated at 70.degree. C. for 20 minutes to give a dark brown solution. 5-Iodo-3'-**deoxyuridine** (5.0 g, 14.1 mmol) and methyl 2,4-pentadienoate (2.5 g, 22.3 mmol) were added and the mixture was heated under reflux. . .

DETD 5-(2-Bromovinyl)-2'-**deoxyuridine** phenyl N-methoxy-L-alaninyl phosphoramidate (NB1011)

DETD [0269] The reaction was performed under argon atmosphere. 5-(2-bromovinyl)-2'-**deoxyuridine** (BVdU) (204 g; 612 mmol) was placed in three-neck 3 liter round bottom flask equipped with mechanical stirrer. The flask. . .

DETD [0272] 5-(4,4-dibromo-1,3-butadienyl)-2'-**deoxyuridine**;

DETD [0273] 5-(2-chlorovinyl)-2'-**deoxyuridine**;

DETD [0274] 5-trifluoromethyl-2'-**deoxyuridine**;

DETD [0275] 5-(4-carbethoxy-1,3-butadienyl)-2'-**deoxyuridine**;

DETD [0277] 5-(4-bromo-1E,3E-butadienyl)-2'-**deoxyuridine**;

DETD [0278] 5-(4-bromo-1E,3Z-butadienyl)-2'-**deoxyuridine**;

DETD [0279] 5-(trimethylsilylethynyl)-2'-**deoxyuridine**;

DETD [0280] 5-(ethynyl)-2'-**deoxyuridine**;

DETD [0281] 5-(1-decynyl)-2'-**deoxyuridine**;

DETD [0284] Using the methods described in Examples 14 and 15, the following amino acid phosphoramidate derivatives of 5-(2-bromovinyl)-2'-**deoxyuridine** were prepared:

DETD . . . Immediately prior to the thymidylate synthase assay, the media was replaced with RPMI+10% dialyzed fetal calf serum. 0.5 .mu.Ci of 5-[.sup.3H]**deoxyuridine** was added to each well, and plates were incubated for 60 minutes at 37.degree. C. without additional CO.sub.2. [.sup.3H] release was measured by adsorbing 5-[.sup.3H] **deoxyuridine** to activated charcoal (10% in 1.times.PBS) for 5 minutes at room temperature. After centrifugation for 5 minutes at 13,000 RPM,. . .

DETD . . . milieu. In order to further explore this question, cell-based assays for TS activity were performed. In these experiments exogenous 5-(3H) **deoxyuridine** is added to cell culture medium and the release of tritiated water is monitored (Carreras, C. W. and Santi, D.. . .

DETD . . . release from .sup.3H-dUMP. These assays were chosen because antibody-detection is commonly used for clinical samples and tritium release from labeled **deoxyuridine** is a direct measure of TS catalytic activity in cells.

DETD . . . has been shown to be predictive for clinical success in the development of new agents to treat inflammatory disease, especially **rheumatoid arthritis** (Elliott et al. (1994) and Feldmann et al. (1998)). This model therefore represents an ideal

setting for establishing proof of concept for new agents to treat **rheumatoid arthritis**, and potentially other autoimmune and inflammatory diseases.

DETD . . . to anti-angiogenesis agents, an anti-CD4 immunosuppressive agent, and cannabidiol, a third experimental agent currently being considered for use to treat **rheumatoid arthritis**, and potentially other autoimmune and inflammatory disorders (Malfait, A. M. et al. (2000); Miotla, J. et al. (2000); Marinova-Mutafchieva, L.. . .

L7 ANSWER 3 OF 3 USPATFULL
AN 2002:273391 USPATFULL
TI Methods to treat autoimmune and inflammatory conditions
IN Shepard, H. Michael, Encinitas, CA, UNITED STATES
PI US 2002151519 A1 20021017
AI US 2002-51320 A1 20020118 (10)
PRAI US 2001-262849P 20010119 (60)
DT Utility
FS APPLICATION
LREP McCutchen, Doyle, Brown & Enersen LLP, Suite 1800, Three Embarcadero Center, San Francisco, CA, 94111
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 1850
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . the affected cell or tissue with a therapeutic compound as described herein. Such pathologies include, but are not limited to **rheumatoid arthritis**, systemic lupus erythmatosus, psoriatic arthritis, reactive arthritis, Crohn's disease, ulcerative colitis and scleroderma. Therapeutic compounds useful in the methods of. . .

SUMM . . . (Cordan-Cardo, C. and Prives, C. (1999)) and/or defective apoptosis (programmed cell death) (Mountz, J. D. et al. (1994)). These include: **rheumatoid arthritis**, systemic lupus erythmatosus, psoriatic arthritis, reactive arthritis, Crohn's disease, ulcerative colitis and scleroderma. Table 1 lists literature examples which suggest. . . Suppressor Mutation/Inactivation Relates to Noncancer Hyperproliferative Disease, Autoimmune Disease and Inflammation.

Impact	Disease Effect	Reference
Increased IL6	Proliferation	Han et al. (1999)
	Inflammation **Rheumatoid Arthritis**	
Increased metalloproteinases	Tissue Degradation	Sun, Y. et al. (2000)
Increased proliferation of synovial cells	**Rheumatoid arthritis**	Aupperle, K. R. et al. (1998)
Genetic instability and disease progression	Chronic inflammation Ulcerative colitis. . .	Tak. P. P. et al. (2000)

SUMM [0009] The methods are useful to treat or ameliorate the symptoms of autoimmune diseases, for example, systemic lupus erythematosus, **rheumatoid arthritis**, psoriatic arthritis, reactive arthritis, Sjogren's syndrome, graft-versus-host disease (GVHD), myasthenia gravis, atherosclerosis, glomerulonephritis, Type 1 diabetes, muscular dystrophy and osteoarthritis.. . .

DRWD [0010] FIG. 1 shows clinical scoring of animals with collagen-induced arthritis using NB 1011, a 5'-**phosphoramidatyl**

deoxyuridine derivate and controls.

DETD . . . produces antibodies or immune cells which recognize the organism's own molecules, cells or tissues. Non-limiting examples of autoimmune disorders include **rheumatoid arthritis**, Sjogren's syndrome, graft versus host disease, myasthenia gravis, and systemic lupus erythematosus.

DETD . . . inflammatory diseases include Crohn's disease, psoriasis, and asthma, are also included within the term "inflammatory condition." Autoimmune diseases such as **rheumatoid arthritis** and systemic lupus erythematosus can also result in a chronic inflammatory state.

DETD . . . substituted acyclic and unsubstituted acyclic. The 1,5-substituted pyrimidine derivative or analog includes, but is not limited to, a 5'-phosphoryl, 5-substituted **deoxyuridine** derivative or analog or a 5'-phosphoramidate, 5-substituted **deoxyuridine** derivative or analog. More specifically, the 1,5-substituted pyrimidine derivative or analog includes, but is not limited to, (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alanylphosphoramidate.. . .

DETD [0035] In one aspect, the disease is an autoimmune disease, for example, psoriatic arthritis, atherosclerosis, reactive arthritis, systemic lupus erythematosus, **rheumatoid arthritis**, Sjogren's syndrome, graft-versus-host disease, osteoarthritis, glomerulonephritis, Type 1 diabetes, muscular dystrophy, or myasthenia gravis. In another aspect, the disease is. . .

DETD . . . suitable cells or tissue ("control sample") with an effective amount of a compound selected from the group consisting of a **deoxyuridine**, a substituted **deoxyuridine**, a substituted **deoxyuridine** derivative and analogs thereof and contacting a second sample of the suitable cells or tissue ("test sample") with the agent. . .

DETD . . . substituted acyclic and unsubstituted acyclic. The 1,5-substituted pyrimidine derivative or analog includes, but is not limited to, a 5'-phosphoryl, 5-substituted **deoxyuridine** derivative or analog or a 5'-phosphoramidate, 5-substituted **deoxyuridine** derivative or analog. More specifically, the 1,5-substituted pyrimidine derivative or analog includes, but is not limited to, (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alanylphosphoramidate.

DETD [0147] One method requires treatment of 5-chloromercuri-2'-**deoxyuridine** with haloalkyl compounds, haloacetates or haloalkenes in the presence of Li.sub.2PdCl.sub.4 to form, through an organopalladium intermediate, the 5-alkyl, 5-acetyl. . .

DETD . . . monophosphate, 5' phosphodiester, or 5' protected ("masked") deoxyuridines or comparable derivatives of alternative carbohydrate moieties, as described below. Protected 5-substituted **deoxyuridine** monophosphate derivatives are those in which the phosphate moiety has been blocked through the attachment of suitable chemical protecting groups.. . .

DETD [0157] Closely following the literature procedures, a t-butyldimethylsilyl propargyl ether-equipped 3', 5'-di-O-protected 2'-**deoxyuridine** (Graham, D. et al. (1998), and De Clercq, E. et al. (1983)) can be prepared and a portion of it,. . .

DETD [0160] Synthesis of furano-pyrimidinones begins with synthesis of a C5 propargylic--alcohol-equipped 2'-**deoxyuridine**. Furano-pyrimidinone compounds are then be formed from the O-tetrahydropyranyl ether derivative described above. Synthesis proceeds by reaction of the second. . .

DETD [0161] Furo[2,3-d]pyrimidinone nucleosides (represented by the above generic structure) were prepared by condensing 2',3'-di-O-p-toluoyl or 2',3'-di-O-acetyl-5-iodo-2'-**deoxyuridine** with 1-(tetrahydropyranyloxy)-2-propyne (Jones, R. G. and Mann, M. J. (1953))

under conditions known to promote the formation of these fluorescent. . .

DETD . . . leaving groups to either the C6 fluoro-uridine base or the C4 hydrazone modified pyrimidine. Methods described above for synthesis of 2-**deoxyuridine** based compounds can again be employed for the synthesis of such molecules.

DETD [0180] The 4-nitrophenyl ether derivative of 5-(3-hydroxy-1-propynyl)-2'-**deoxyuridine** was prepared according to standard ether synthesis as shown below. ##STR44##

DETD 5-[3-(4-Nitrophenoxy)-1-propynyl]-2'-**deoxyuridine**

DETD [0181] A solution of pre-dried 5-(3-hydroxy-1-propynyl)-2'-**deoxyuridine** (Robins, M. J. et al. (1983)) (565 mg, 2 mmol) in 40 mL of anhydrous THF under argon was treated. . .

DETD [0182] (a) 5-(Carbomethoxyvinyl)-2 '-**deoxyuridine** -3',5'-bis(tetrahydro-2H-pyran-2-yl)ether (I)

DETD [0183] A slurry of 5-(carbomethoxyvinyl)-2'-**deoxyuridine** (3.0 g, 9.6 mmol), 3,4-dihydro-2H-pyran (22 mL, 21.3 mmol) and pyridinium p-toluenesulfonate (PPTS, 0.242 g, 0.96 mmol) in dimethylformamide (DMF,. . .

DETD [0184] (b) 5-(3-Hydroxyprop-1-enyl)-2'-**deoxyuridine** -3',5'-bis(tetrahydro-2H-pyran-2-yl)ether (II)

DETD . . . were added and the solution was heated at 70.degree. C. for 20 minutes to give a dark brown solution. 5-Iodo-3 '-**deoxyuridine** (5.0 g, 14.1 mmol) and methyl 2,4-pentadienoate (2.5 g, 22.3 mmol) were added and the mixture was heated under reflux. . .

DETD [0207] 5-(2-Bromovinyl)-2'-**deoxyuridine** phenyl N-methoxy-L-alaninyl phosphoramidate (NB1011)

DETD [0208] The reaction was performed under argon atmosphere. 5-(2-bromovinyl)-2'-**deoxyuridine** (BVdU) (204 g; 612 mmol) was placed in three-neck 3 liter round bottom flask equipped with mechanical stirrer. The flask. . .

DETD [0211] 5-(4,4-dibromo-1,3-butadienyl)-2'-**deoxyuridine**;

DETD [0212] 5-(2-chlorovinyl)-2'-**deoxyuridine**;

DETD [0213] 5-trifluoromethyl-2'-**deoxyuridine**;

DETD [0214] 5-(4-carbethoxy-1,3-butadienyl)-2'-**deoxyuridine**;

DETD [0216] 5-(4-bromo-1E,3E-butadienyl)-2'-**deoxyuridine**;

DETD [0217] 5-(4-bromo-1E,3Z-butadienyl)-2'-**deoxyuridine**;

DETD [0218] 5-(trimethylsilylethynyl)-2'-**deoxyuridine**;

DETD [0219] 5-(ethynyl)-2'-**deoxyuridine**;

DETD [0220] 5-(1-decynyl)-2'-**deoxyuridine**;

DETD . . . has been shown to be predictive for clinical success in the development of new agents to treat inflammatory disease, especially **rheumatoid arthritis** (Elliott et al. (1994); Feldmann et al. (1998)). This model therefore represents an ideal setting for establishing proof of concept for new agents to treat **rheumatoid arthritis**, and potentially other autoimmune and inflammatory diseases.

DETD . . . to anti-angiogenesis agents, an anti-CD4 immunosuppressive agent, and cannabidiol, a third experimental agent currently being considered for use to treat **rheumatoid arthritis**, and potentially other autoimmune and inflammatory disorders (Malfait, A. M. et al. (2000); Miotla, J. et al. (2000); Marinova-Mutafchieva, L.. .

CLM What is claimed is:

2. The method of claim 1, wherein the compound is a 1,5-substituted **deoxyuridine** derivative or analog.

4. The method of claim 2, wherein the 1,5-substituted **deoxyuridine** derivative or analog is a compound selected from the group consisting of a 5'-**phosphoramidatyl deoxyuridine**, a substituted 5'-phosphoramidyl **deoxyuridine**, a 5'-phosphoryl **deoxyuridine**, and a

substituted, 5'-phosphoryl **deoxyuridine**.

5. The method of claim 2, wherein the 1,5-substituted **deoxyuridine** is substituted at the 5 position with a substituent selected from the group consisting of alkyl, alkenyl, alkynyl, vinyl, propargyl. . .
7. The method of claim 6, wherein the halogen-substituted derivative is a 5-haloalkyl substituted **deoxyuridine**.

8. The method of claim 7, wherein the compound is 5-bromovinyl substituted **deoxyuridine**.

9. The method of claim 4, wherein the 1,5-substituted **deoxyuridine** is a 5'-phosphoryl derivative of pyrimidine.

10. The method of claim 4, wherein the 1,5-substituted **deoxyuridine** is a 5'-**phosphoramidatyl** derivative of pyrimidine.

11. The method of claim 10, wherein the a 5'-**phosphoramidatyl** derivative is (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate.

. . . wherein the autoimmune disease is selected from the group consisting of multiple sclerosis, Type 1 diabetes, glomerulonephotis systemic lupus erythematosus, **rheumatoid arthritis**, psoriatic arthritis, reactive arthritis, Sjogren's syndrome, graft-versus-host disease (GVHD), muscular dystrophy, myasthenia gravis, atherosclerosis and osteoarthritis.

. . . sample comprising suitable cells or tissue with an effective amount of a compound selected from the group consisting of a **deoxyuridine**, a substituted **deoxyuridine**, a substituted **deoxyuridine** derivative and analogs thereof and contacting a second sample of the suitable cells or tissue with the agent to be. . .
22. The assay of claim 21, wherein the substituted **deoxyuridine** derivative is (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate.

L7 ANSWER 1 OF 3 IFIPAT COPYRIGHT 2003 IFI
AN 10207812 IFIPAT;IFIUDB;IFICDB
TI METHODS TO TREAT AUTOIMMUNE AND INFLAMMATORY CONDITIONS
INF Shepard; H. Michael, Encinitas, CA, US
IN Shepard H Michael
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG McCutchen, Doyle, Brown & Enersen LLP, Suite 1800, Three Embarcadero Center, San Francisco, CA, 94111, US
PI US 2002151519 A1 20021017
AI US 2002-51320 20020118
PRAI US 2001-262849P 20010119 (Provisional)
FI US 2002151519 20021017
DT Utility; Patent Application - First Publication
FS CHEMICAL
APPLICATION
CLMN 22
GI 3 Figure(s).
FIG. 1 shows clinical scoring of animals with collagen-induced arthritis using NB 1011, a 5'-**phosphoramidatyl deoxyuridine** derivate and controls.

FIG. 2 shows therapeutic effect on paw swelling in animals with collagen-induced arthritis.

FIG. 3 shows histological evaluation of all joints performed by an observer blinded to the treatments received. This figure represents the percentage of joints exhibiting normal, mild or moderate to severe arthritic changes in the joint architecture in different treatment groups. Chi-square test (2 x 2 correlation) was done to calculate statistical significance of data. P less-than 0.05 (*) was considered significant.

AB . . . the affected cell or tissue with a therapeutic compound as described herein. Such pathologies include, but are not limited to **rheumatoid arthritis**, systemic lupus erythmatosus, psoriatic arthritis, reactive arthritis, Crohn's disease, ulcerative colitis and scleroderma. Therapeutic compounds useful in the methods of. . .

GI 3 Figure(s).

FIG. 1 shows clinical scoring of animals with collagen-induced arthritis using NB 1011, a 5'-**phosphoramidatyl deoxyuridine** derivate and controls.

FIG. 2 shows therapeutic effect on paw swelling in animals with collagen-induced arthritis.

FIG. 3 shows histological evaluation of. . .

ACLM 2. The method of claim 1, wherein the compound is a 1,5-substituted **deoxyuridine** derivative or analog.

4. The method of claim 2, wherein the 1,5-substituted **deoxyuridine** derivative or analog is a compound selected from the group consisting of a 5'-**phosphoramidatyl deoxyuridine**, a substituted 5'-phosphoramidyl **deoxyuridine**, a 5'-phosphoryl **deoxyuridine**, and a substituted, 5'-phosphoryl **deoxyuridine**.

5. The method of claim 2, wherein the 1,5-substituted **deoxyuridine** is substituted at the 5 position with a substituent selected from the group consisting of alkyl, alkenyl, alkynyl, vinyl, propargyl. . .

7. The method of claim 6, wherein the halogen-substituted derivative is a 5-haloalkyl substituted **deoxyuridine**.

8. The method of claim 7, wherein the compound is 5-bromovinyl substituted **deoxyuridine**.

9. The method of claim 4, wherein the 1,5-substituted **deoxyuridine** is a 5'-phosphoryl derivative of pyrimidine.

10. The method of claim 4, wherein the 1,5-substituted **deoxyuridine** is a 5'-**phosphoramidatyl** derivative of pyrimidine.

11. The method of claim 10, wherein the a 5'-**phosphoramidatyl** derivative is (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate.

. . . wherein the autoimmune disease is selected from the group consisting of multiple sclerosis, Type 1 diabetes, glomerulonephotis systemic lupus erythematosus, **rheumatoid arthritis**, psoriatic arthritis, reactive arthritis, Sjogren's syndrome, graft-versus-host disease (GVHD), muscular dystrophy, myasthenia gravis, atherosclerosis and osteoarthritis.

. . . sample comprising suitable cells or tissue with an effective amount of a compound selected from the group consisting of a **deoxyuridine**, a substituted **deoxyuridine**, a substituted **deoxyuridine** derivative and analogs thereof and contacting a second sample of the suitable cells or tissue with the agent to be. . .

22. The assay of claim 21, wherein the substituted **deoxyuridine** derivative is (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate.

L7 ANSWER 2 OF 3 USPATFULL

AN 2003:160082 USPATFULL
TI Novel phosphoramidate compounds and methods of use
IN Shepard, H. Michael, Encinitas, CA, UNITED STATES
Vaino, Andrew Rein, San Diego, CA, UNITED STATES
Lehsten, Danielle M., San Diego, CA, UNITED STATES
PI US 2003109697 A1 20030612
AI US 2002-119927 A1 20020409 (10)
RLI Continuation-in-part of Ser. No. US 2001-782721, filed on 12 Feb 2001, PENDING Continuation of Ser. No. US 1999-235961, filed on 22 Jan 1999, GRANTED, Pat. No. US 6339151
PRAI US 1998-72264P 19980123 (60)
US 1998-76950P 19980305 (60)
US 1998-108634P 19981116 (60)
DT Utility
FS APPLICATION
LREP McCutchen, Doyle, Brown & Enersen LLP, Suite 1800, Three Embarcadero Center, San Francisco, CA, 94111
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 10 Drawing Page(s)
LN.CNT 3503
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB . . . cancer, infectious disease, an autoimmune disorder or an inflammatory condition. Therapeutic compounds useful in the methods of this invention are 5'-**phosphoramidatyl**, 1,5-substituted pyrimidine compounds, derivatives, analogs and pharmaceutically acceptable salts thereof
SUMM . . . (Cordan-Cardo, C. and Prives, C. (1999)) and/or defective apoptosis (programmed cell death) (Mountz, J. D. et al. (1994)). These include: **rheumatoid arthritis**, systemic lupus erythmatosus, psoriatic arthritis, reactive arthritis, Crohn's disease, ulcerative colitis and scleroderma. Table 1 lists literature examples which suggest. . . Tumor
Suppressor Mutation/Inactivation Relates to Noncancer Hyperproliferative Disease,
Autoimmune Disease and Inflammation.

Impact	Disease Effect	Reference
Increased IL6	Proliferation	Han, et al. (1999)
	Inflammation **Rheumatoid Arthritis**	
Increased metalloproteinases	Tissue Degradation	Sun, Y. et al. (2000)
Increased proliferation of	**Rheumatoid arthritis**	Aupperle, K. R. et al. (1998)
synovial cells		
Genetic instability	Chronic inflammation	Tak, P. P. et al. (2000)
and disease progression	Ulcerative colitis. . .	

SUMM [0013] Novel **phosphoramidatyl**, 1,5-substituted pyrimidine compounds, derivatives, analogs, and pharmaceutically acceptable salts thereof and compositions containing the compounds are provided by this invention.. . .
SUMM . . . or an inflammatory condition, by delivering to the subject an effective amount of at least one or more of the 5'-**phosphoramidatyl**, 1,5-substituted pyrimidine, derivative, analog or pharmaceutically acceptable salt thereof. Methods for synthesizing the compounds are described herein and in Applicants'. . .
DRWD [0020] FIG. 1 is a graph showing fluorescent products from incubation of Bromovinyl, 2'-**Deoxyuridine** Monophosphate ("BVdUMP") with

Recombinant Human Thymidylate Synthase ("rHuTS"). Incubation of BVdUMP with thymidylate synthase ("TS") results in a time and. . .

DRWD . . . activity in intact cells is completely reversible. TS activity was measured in intact RKO cells by release of [.sup.3H].sub.2O from 5-[.sup.3H]**deoxyuridine** as described in Materials and Methods. NB1011 was washed out of cells by replacing with fresh media, incubating for 60. . .

DRWD . . . produces antibodies or immune cells which recognize the organism's own molecules, cells or tissues. Non-limiting examples of autoimmune disorders include **rheumatoid arthritis**, Sjogren's syndrome, graft versus host disease, myasthenia gravis, and systemic lupus erythematosus.

DRWD . . . inflammatory diseases include Crohn's disease, psoriasis, and asthma, are also included within the term "inflammatory condition." Autoimmune diseases such as **rheumatoid arthritis** and systemic lupus erythematosus can also result in a chronic inflammatory state.

DRWD [0080] Therapeutic compounds for use in the methods of this invention are one or more 5'-**phosphoramidatyl** 1,5-substituted pyrimidines, derivatives, analogs or pharmaceutically acceptable salts thereof. The compounds of this invention are nucleoside analogs comprising a substituted. . .

DRWD [0210] One method requires treatment of 5-chloromercuri-2'-**deoxyuridine** with haloalkyl compounds, haloacetates or haloalkenes in the presence of Li.sub.2PdCl.sub.4 to form, through an organopalladium intermediate, the 5-alkyl, 5-acetyl. . .

DRWD . . . monophosphate, 5' phosphodiester, or 5' protected ("masked") deoxyuridines or comparable derivatives of alternative carbohydrate moieties, as described below. Protected 5-substituted **deoxyuridine** monophosphate derivatives are those in which the phosphate moiety has been blocked through the attachment of suitable chemical protecting groups.. . .

DRWD [0220] Closely following the literature procedures, a t-butyldimethylsilyl propargyl ether-equipped 3', 5'-di-O-protected 2'-**deoxyuridine** (Graham, D. et al. (1998), and De Clercq, E. et al. (1983)) can be prepared and a portion of it,. . .

DRWD [0223] Synthesis of furano-pyrimidinones begins with synthesis of a C5 propargylic--alcohol-equipped 2'-**deoxyuridine**. Furano-pyrimidinone compounds are then be formed from the O-tetrahydropyranyl ether derivative described above. Synthesis proceeds by reaction of the second. . .

DRWD [0224] Furo[2,3-d]pyrimidinone nucleosides (represented by the above generic structure) were prepared by condensing 2',3'-di-O-p-toluoyl or 2',3'-di-O-acetyl-5-iodo-2'-**deoxyuridine** with 1-(tetrahydropyranyloxy)-2-propyne (Jones, R. G. and Mann, M. J. (1953)) under conditions known to promote the formation of these fluorescent. . .

DRWD . . . leaving groups to either the C6 fluoro-uridine base or the C4 hydrazone modified pyrimidine. Methods described above for synthesis of 2-**deoxyuridine** based compounds can again be employed for the synthesis of such molecules.

DETD [0243] The 4-nitrophenyl ether derivative of 5-(3-hydroxy-1-propynyl)-2'-**deoxyuridine** was prepared according to standard ether synthesis as shown below. ##STR42##

DETD 5-[3-(4-Nitrophenoxy)-1-propynyl]-2'-**deoxyuridine**

DETD [0244] A solution of pre-dried 5-(3-hydroxy-1 -propynyl)-2'-**deoxyuridine** (Robins, M. J. et al. (1983)) (565 mg, 2 mmol) in 40 mL of anhydrous THF under argon was treated. . .

DETD [0245] (a) 5-(Carbomethoxyvinyl)-2'-**deoxyuridine** -3',5'-bis(tetrahydro-2H-pyran-2-yl)ether (I)

DETD [0246] A slurry of 5-(carbomethoxyvinyl)-2'-**deoxyuridine** (3.0 g, 9.6 mmol), 3,4-dihydro-2H-pyran (22 mL, 21.3 mmol) and pyridinium

p-toluenesulfonate (PPTS, 0.242 g, 0.96 mmol) in dimethylformamide (DMF,. . .

DETD [0247] (b) 5-(3-Hydroxyprop-1-enyl)-2'-**deoxyuridine**-3',5'-bis(tetrahydro-2H-pyran-2-yl)ether (II)

DETD . . . mmol) were added and the solution was heated at 70.degree. C. for 20 minutes to give a dark brown solution. 5-Iodo-3'-**deoxyuridine** (5.0 g, 14.1 mmol) and methyl 2,4-pentadienoate (2.5 g, 22.3 mmol) were added and the mixture was heated under reflux. . .

DETD 5-(2-Bromovinyl)-2'-**deoxyuridine** phenyl N-methoxy-L-alaninyl phosphoramidate (NB1011)

DETD [0269] The reaction was performed under argon atmosphere. 5-(2-bromovinyl)-2'-**deoxyuridine** (BVdU) (204 g; 612 mmol) was placed in three-neck 3 liter round bottom flask equipped with mechanical stirrer. The flask. . .

DETD [0272] 5-(4,4-dibromo-1,3-butadienyl)-2'-**deoxyuridine**;

DETD [0273] 5-(2-chlorovinyl)-2'-**deoxyuridine**;

DETD [0274] 5-trifluoromethyl-2'-**deoxyuridine**;

DETD [0275] 5-(4-carbethoxy-1,3-butadienyl)-2'-**deoxyuridine**;

DETD [0277] 5-(4-bromo-1E,3E-butadienyl)-2'-**deoxyuridine**;

DETD [0278] 5-(4-bromo-1E,3Z-butadienyl)-2'-**deoxyuridine**;

DETD [0279] 5-(trimethylsilylethynyl)-2'-**deoxyuridine**;

DETD [0280] 5-(ethynyl)-2'-**deoxyuridine**;

DETD [0281] 5-(1-decynyl)-2'-**deoxyuridine**;

DETD [0284] Using the methods described in Examples 14 and 15, the following amino acid phosphoramidate derivatives of 5-(2-bromovinyl)-2'-**deoxyuridine** were prepared:

DETD . . . Immediately prior to the thymidylate synthase assay, the media was replaced with RPMI+10% dialyzed fetal calf serum. 0.5 .mu.Ci of 5-[.sup.3H]**deoxyuridine** was added to each well, and plates were incubated for 60 minutes at 37.degree. C. without additional CO.sub.2. [.sup.3H] release was measured by adsorbing 5-[.sup.3H] **deoxyuridine** to activated charcoal (10% in 1.times.PBS) for 5 minutes at room temperature. After centrifugation for 5 minutes at 13,000 RPM,. . .

DETD . . . milieu. In order to further explore this question, cell-based assays for TS activity were performed. In these experiments exogenous 5-(3H) **deoxyuridine** is added to cell culture medium and the release of tritiated water is monitored (Carreras, C. W. and Santi, D.. . .

DETD . . . release from .sup.3H-dUMP. These assays were chosen because antibody-detection is commonly used for clinical samples and tritium release from labeled **deoxyuridine** is a direct measure of TS catalytic activity in cells.

DETD . . . has been shown to be predictive for clinical success in the development of new agents to treat inflammatory disease, especially **rheumatoid arthritis** (Elliott et al. (1994) and Feldmann et al. (1998)). This model therefore represents an ideal setting for establishing proof of concept for new agents to treat **rheumatoid arthritis**, and potentially other autoimmune and inflammatory diseases.

DETD . . . to anti-angiogenesis agents, an anti-CD4 immunosuppressive agent, and cannabidiol, a third experimental agent currently being considered for use to treat **rheumatoid arthritis**, and potentially other autoimmune and inflammatory disorders (Malfait, A. M. et al. (2000); Miotla, J. et al. (2000); Marinova-Mutafchieva, L.. . .

L7 ANSWER 3 OF 3 USPATFULL

AN 2002:273391 USPATFULL

TI Methods to treat autoimmune and inflammatory conditions

IN Shepard, H. Michael, Encinitas, CA, UNITED STATES

PI US 2002151519 A1 20021017
AI US 2002-51320 A1 20020118 (10)
PRAI US 2001-262849P 20010119 (60)
DT Utility
FS APPLICATION
LREP McCutchen, Doyle, Brown & Enersen LLP, Suite 1800, Three Embarcadero Center, San Francisco, CA, 94111
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 1850
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . the affected cell or tissue with a therapeutic compound as described herein. Such pathologies include, but are not limited to **rheumatoid arthritis**, systemic lupus erythmatosus, psoriatic arthritis, reactive arthritis, Crohn's disease, ulcerative colitis and scleroderma. Therapeutic compounds useful in the methods of. . .

SUMM . . . (Cordan-Cardo, C. and Prives, C. (1999)) and/or defective apoptosis (programmed cell death) (Mountz, J. D. et al. (1994)). These include: **rheumatoid arthritis**, systemic lupus erythmatosus, psoriatic arthritis, reactive arthritis, Crohn's disease, ulcerative colitis and scleroderma. Table 1 lists literature examples which suggest. . . Suppressor Mutation/Inactivation Relates to Noncancer Hyperproliferative Disease, Autoimmune Disease and Inflammation.

Impact	Disease Effect	Reference
Increased IL6	Proliferation	Han et al. (1999)
	Inflammation	
	Rheumatoid Arthritis	
Increased metalloproteinases	Tissue Degradation	Sun, Y. et al. (2000)
Increased proliferation of	**Rheumatoid arthritis**	Aupperle, K. R. et al.
synovial cells		(1998)
Genetic instability	Chronic inflammation	Tak. P. P. et al. (2000)
and disease progression	Ulcerative colitis. . .	

SUMM [0009] The methods are useful to treat or ameliorate the symptoms of autoimmune diseases, for example, systemic lupus erythematosus, **rheumatoid arthritis**, psoriatic arthritis, reactive arthritis, Sjogren's syndrome, graft-versus-host disease (GVHD), myasthenia gravis, atherosclerosis, glomerulonephritis, Type 1 diabetes, muscular dystrophy and osteoarthritis.. . .

DRWD [0010] FIG. 1 shows clinical scoring of animals with collagen-induced arthritis using NB 1011, a 5'-**phosphoramidatyl deoxyuridine** derivate and controls.

DETD . . . produces antibodies or immune cells which recognize the organism's own molecules, cells or tissues. Non-limiting examples of autoimmune disorders include **rheumatoid arthritis**, Sjogren's syndrome, graft versus host disease, myasthenia gravis, and systemic lupus erythematosus.

DETD . . . inflammatory diseases include Crohn's disease, psoriasis, and asthma, are also included within the term "inflammatory condition." Autoimmune diseases such as **rheumatoid arthritis** and systemic lupus erythematosus can also result in a chronic inflammatory state.

DETD . . . substituted acyclic and unsubstituted acyclic. The 1,5-substituted pyrimidine derivative or analog includes, but is not limited to, a 5'-phosphoryl, 5-substituted **deoxyuridine**

derivative or analog or a 5'-phosphoramidate, 5-substituted **deoxyuridine** derivative or analog. More specifically, the 1,5-substituted pyrimidine derivative or analog includes, but is not limited to, (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alanylphosphoramidate.. . .

DETD [0035] In one aspect, the disease is an autoimmune disease, for example, psoriatic arthritis, atherosclerosis, reactive arthritis, systemic lupus erythematosus, **rheumatoid arthritis**, Sjogren's syndrome, graft-versus-host disease, osteoarthritis, glomerulonephritis, Type 1 diabetes, muscular dystrophy, or myasthenia gravis. In another aspect, the disease is. . .

DETD . . . suitable cells or tissue ("control sample") with an effective amount of a compound selected from the group consisting of a **deoxyuridine**, a substituted **deoxyuridine**, a substituted **deoxyuridine** derivative and analogs thereof and contacting a second sample of the suitable cells or tissue ("test sample") with the agent. . .

DETD . . . substituted acyclic and unsubstituted acyclic. The 1,5-substituted pyrimidine derivative or analog includes, but is not limited to, a 5'-phosphoryl, 5-substituted **deoxyuridine** derivative or analog or a 5'-phosphoramidate, 5-substituted **deoxyuridine** derivative or analog. More specifically, the 1,5-substituted pyrimidine derivative or analog includes, but is not limited to, (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alanylphosphoramidate.

DETD [0147] One method requires treatment of 5-chloromercuri-2'-**deoxyuridine** with haloalkyl compounds, haloacetates or haloalkenes in the presence of Li.sub.2PdCl.sub.4 to form, through an organopalladium intermediate, the 5-alkyl, 5-acetyl. . .

DETD . . . monophosphate, 5' phosphodiester, or 5' protected ("masked") deoxyuridines or comparable derivatives of alternative carbohydrate moieties, as described below. Protected 5-substituted **deoxyuridine** monophosphate derivatives are those in which the phosphate moiety has been blocked through the attachment of suitable chemical protecting groups.. . .

DETD [0157] Closely following the literature procedures, a t-butyldimethylsilyl propargyl ether-equipped 3', 5'-di-O-protected 2'-**deoxyuridine** (Graham, D. et al. (1998), and De Clercq, E. et al. (1983)) can be prepared and a portion of it,. . .

DETD [0160] Synthesis of furano-pyrimidinones begins with synthesis of a C5 propargylic--alcohol-equipped 2'-**deoxyuridine**. Furano-pyrimidinone compounds are then be formed from the O-tetrahydropyranyl ether derivative described above. Synthesis proceeds by reaction of the second. . .

DETD [0161] Furo[2,3-d]pyrimidinone nucleosides (represented by the above generic structure) were prepared by condensing 2',3'-di-O-p-toluoyl or 2',3'-di-O-acetyl-5-iodo-2'-**deoxyuridine** with 1-(tetrahydropyranyloxy)-2-propyne (Jones, R. G. and Mann, M. J. (1953)) under conditions known to promote the formation of these fluorescent. . .

DETD . . . leaving groups to either the C6 fluoro-uridine base or the C4 hydrazone modified pyrimidine. Methods described above for synthesis of 2-**deoxyuridine** based compounds can again be employed for the synthesis of such molecules.

DETD [0180] The 4-nitrophenyl ether derivative of 5-(3-hydroxy-1-propynyl)-2'-**deoxyuridine** was prepared according to standard ether synthesis as shown below. ##STR44##

DETD 5-[3-(4-Nitrophenoxy)-1-propynyl]-2'-**deoxyuridine**

DETD [0181] A solution of pre-dried 5-(3-hydroxy-1-propynyl)-2'-**deoxyuridine** (Robins, M. J. et al. (1983)) (565 mg, 2 mmol) in 40 mL of anhydrous THF under argon was treated. . .

DETD [0182] (a) 5-(Carbomethoxyvinyl)-2 '-**deoxyuridine**

-3',5'-bis(tetrahydro-2H-pyran-2-yl)ether (I)

DETD [0183] A slurry of 5-(carbomethoxyvinyl)-2'-**deoxyuridine** (3.0 g, 9.6 mmol), 3,4-dihydro-2H-pyran (22 mL, 21.3 mmol) and pyridinium p-toluenesulfonate (PPTS, 0.242 g, 0.96 mmol) in dimethylformamide (DMF,. . .

DETD [0184] (b) 5-(3-Hydroxyprop-1-enyl)-2'-**deoxyuridine** -3',5'-bis(tetrahydro-2H-pyran-2-yl)ether (II)

DETD . . . were added and the solution was heated at 70.degree. C. for 20 minutes to give a dark brown solution. 5-Iodo-3 '-**deoxyuridine** (5.0 g, 14.1 mmol) and methyl 2,4-pentadienoate (2.5 g, 22.3 mmol) were added and the mixture was heated under reflux. . .

DETD [0207] 5-(2-Bromovinyl)-2'-**deoxyuridine** phenyl N-methoxy-L-alaninyl phosphoramidate (NB1011)

DETD [0208] The reaction was performed under argon atmosphere. 5-(2-bromovinyl)-2'-**deoxyuridine** (BVdU) (204 g; 612 mmol) was placed in three-neck 3 liter round bottom flask equipped with mechanical stirrer. The flask. . .

DETD [0211] 5-(4,4-dibromo-1,3-butadienyl)-2'-**deoxyuridine**;

DETD [0212] 5-(2-chlorovinyl)-2'-**deoxyuridine**;

DETD [0213] 5-trifluoromethyl-2'-**deoxyuridine**;

DETD [0214] 5-(4-carbethoxy-1,3-butadienyl)-2'-**deoxyuridine**;

DETD [0216] 5-(4-bromo-1E,3E-butadienyl)-2'-**deoxyuridine**;

DETD [0217] 5-(4-bromo-1E,3Z-butadienyl)-2'-**deoxyuridine**;

DETD [0218] 5-(trimethylsilylethynyl)-2'-**deoxyuridine**;

DETD [0219] 5-(ethynyl)-2'-**deoxyuridine**;

DETD [0220] 5-(1-decynyl)-2'-**deoxyuridine**;

DETD . . . has been shown to be predictive for clinical success in the development of new agents to treat inflammatory disease, especially **rheumatoid arthritis** (Elliott et al. (1994); Feldmann et al. (1998)). This model therefore represents an ideal setting for establishing proof of concept for new agents to treat **rheumatoid arthritis**, and potentially other autoimmune and inflammatory diseases.

DETD . . . to anti-angiogenesis agents, an anti-CD4 immunosuppressive agent, and cannabidiol, a third experimental agent currently being considered for use to treat **rheumatoid arthritis**, and potentially other autoimmune and inflammatory disorders (Malfait, A. M. et al. (2000); Miotla, J. et al. (2000); Marinova-Mutafchieva, L.. . .

CLM What is claimed is:

2. The method of claim 1, wherein the compound is a 1,5-substituted **deoxyuridine** derivative or analog.

4. The method of claim 2, wherein the 1,5-substituted **deoxyuridine** derivative or analog is a compound selected from the group consisting of a 5'-**phosphoramidatyl deoxyuridine**, a substituted 5'-phosphoramidyl **deoxyuridine**, a 5'-phosphoryl **deoxyuridine**, and a substituted, 5'-phosphoryl **deoxyuridine**.

5. The method of claim 2, wherein the 1,5-substituted **deoxyuridine** is substituted at the 5 position with a substituent selected from the group consisting of alkyl, alkenyl, alkynyl, vinyl, propargyl. . .

7. The method of claim 6, wherein the halogen-substituted derivative is a 5-haloalkyl substituted **deoxyuridine**.

8. The method of claim 7, wherein the compound is 5-bromovinyl substituted **deoxyuridine**.

9. The method of claim 4, wherein the 1,5-substituted **deoxyuridine** is a 5'-phosphoryl derivative of pyrimidine.

10. The method of claim 4, wherein the 1,5-substituted **deoxyuridine** is a 5'-**phosphoramidatyl** derivative of pyrimidine.

11. The method of claim 10, wherein the a 5'-**phosphoramidatyl** derivative is (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate.

. . . wherein the autoimmune disease is selected from the group consisting of multiple sclerosis, Type 1 diabetes, glomerulonephotis systemic lupus erythematosus, **rheumatoid arthritis**, psoriatic arthritis, reactive arthritis, Sjogren's syndrome, graft-versus-host disease (GVHD), muscular dystrophy, myasthenia gravis, atherosclerosis and osteoarthritis.

. . . sample comprising suitable cells or tissue with an effective amount of a compound selected from the group consisting of a **deoxyuridine**, a substituted **deoxyuridine**, a substituted **deoxyuridine** derivative and analogs thereof and contacting a second sample of the suitable cells or tissue with the agent to be. . .
22. The assay of claim 21, wherein the substituted **deoxyuridine** derivative is (E)-5-(2-bromovinyl)-2'-deoxy-5'-uridyl phenyl L-alaninylphosphoramidate.

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=> d his

     (FILE 'HOME' ENTERED AT 11:41:51 ON 08 JUL 2003)

     FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT,
     CAPLUS, CEN, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL,
     EMBASE, ESBIOBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF,
     MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ...' ENTERED AT 11:41:58 ON 08 JUL
     2003
L1         56898 S DEOXYURIDINE
L2           335 S L1 AND RHEUMATOID ARTHRITIS
L3           120 S L2 AND PD<2001
L4             1 S L3 AND PHOSPHORYL
L5             4 S L1 AND PHOSPHORAMIDATYL
L6          1644 S D HIS
L7             3 S L2 AND PHOSPHORAMIDATYL

=> s rheumatoid arthritis
  34 FILES SEARCHED...
L8       602683 RHEUMATOID ARTHRITIS

=> s l8 and 1,5 (4w) pyrimidine
   7 FILES SEARCHED...
  17 FILES SEARCHED...
  24 FILES SEARCHED...
  34 FILES SEARCHED...
L9           76 L8 AND 1,5 (4W) PYRIMIDINE

=> s l9 and pd<2000
   4 FILES SEARCHED...
'2000' NOT A VALID FIELD CODE
   9 FILES SEARCHED...
'2000' NOT A VALID FIELD CODE
'2000' NOT A VALID FIELD CODE
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  16 FILES SEARCHED...
  19 FILES SEARCHED...
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  22 FILES SEARCHED...
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'2000' NOT A VALID FIELD CODE
'2000' NOT A VALID FIELD CODE
  26 FILES SEARCHED...
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'2000' NOT A VALID FIELD CODE
  32 FILES SEARCHED...
  33 FILES SEARCHED...
L10          25 L9 AND PD<2000

=> d l10 1-25 bib, ab

L10  ANSWER 1 OF 25  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN   1988:387294  BIOSIS
DN   BR35:61222
TI   PYRAZOLO-1 5-A-PYRIMIDINE DERIVATIVES AS
     POTENTIAL ANTIARTHRITIC AGENTS.
AU   NUGENT R A; SMITH R J; MURPHY M; ROHLOFF N A; NEPPER S T
CS   DEP. HYPERSENSITIVITY DIS. RES., UPJOHN CO., KALAMAZOO, MI 49001.
SO   THIRD CHEMICAL CONGRESS OF NORTH AMERICA HELD AT THE 195TH AMERICAN
     CHEMICAL SOCIETY MEETING, TORONTO, ONTARIO, CANADA, JUNE 5-10, 1988. ABSTR
     PAP CHEM CONGR NORTH AM. (1988) 3 (2), MEDI 139.
     CODEN: ABPAEK.
DT   Conference
FS   BR; OLD
LA   English

L10  ANSWER 2 OF 25  CAPLUS  COPYRIGHT 2003 ACS
AN   1999:753238  CAPLUS
DN   132:12322
TI   Preparation of pyrazolo[1,5-a]pyrimidine
     derivatives as nitrogen monoxide synthase inhibitors
IN   Okamura, Takashi; Shoji, Yasuo; Shibutani, Tadao; Yasuda, Tsuneo; Iwamoto,
     Takeshi
PA   Otsuka Pharmaceutical Factory, Inc., Japan
SO   PCT Int. Appl., 109 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 9959998         A1   19991125      WO 1999-JP2572   19990517 <--
         W:  AU, CA, CN, JP, KR, NO, US
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
     CA 2331468          AA   19991125      CA 1999-2331468  19990517 <--
     AU 9937320          A1   19991206      AU 1999-37320    19990517 <--
     AU 751337           B2   20020815
     EP 1081149          A1   20010307      EP 1999-919634   19990517
     EP 1081149          B1   20030402
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     AT 236166           E    20030415      AT 1999-919634   19990517
     NO 2000005820       A    20001117      NO 2000-5820     20001117
     US 6372749          B1   20020416      US 2000-700764   20001120
PRAI JP 1998-136960      A    19980519
     WO 1999-JP2572      W    19990517
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OS MARPAT 132:12322
AB Pyrazolo[**1,5**-a]**pyrimidine** derivs. represented by general formula [I; R1 = lower alkyl, Ph, thienyl; one of R2 and R3 = H and the other = naphthyl, furyl, pyridyl, styryl, phenylethynyl, (un)substituted Ph; R4 = H, lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, CO2H, lower alkoxycarbonyl, et.], which have pharmacol. effects including analgesic effect and nitrogen monoxide synthase inhibitory effect and are useful as analgesic agents and remedies and preventives for sepsis, endotoxin shock, chronic **rheumatoid arthritis**, etc., are prepd. Thus, 1.0 g di-Et (5-n-butylpyrazolo[1,5-a]pyrimidin-7-yl)methylphosphonate and 0.66 g 3,4,5-trimethoxybenzaldehyde were dissolved in 5.0 mL ethanol, cooled to 0.degree., treated with 3.8 mL 5% aq. NaOH, and stirred at 0.degree. for 1 h to give the title compd. (I; R1 = n-Bu, R2 = R4 = H, R3 = 3,4,5-trimethoxyphenyl) (II). In an analgesic assay against pressure-stimulated pain, II in vivo showed 47.8% recovery ratio of pain threshold value in the rear sole of rat in 60 min after the treatment with substance P. Pharmaceutical formulation contg. I were also prepd.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2003 ACS
AN 1999:650390 CAPLUS
DN 131:271882
TI Preparation of pyrazolo[1,5-a]pyrimidines as nitrogen monoxide synthase inhibitors
IN Koji, Yasuo; Okamura, Takashi; Hashimoto, Kinji; Kondo, Mitsuyoshi; Shibutani, Naotaka
PA Ohtsuka Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 11279178	A2	19991012	JP 1999-18861	19990127 <--
PRAI JP 1998-17068		19980129		

OS MARPAT 131:271882
AB Title compds. [I; R 1 = CH3(CH2)3, CF3CH2CH2, FCH2CH2, (4-FC6H4)2C:CHCH2, CF3CH2OCH2, OPr-n, OEt, C6H5(CH2)3, C6H5CH2; R2 = H, 2-pyrazinyl; R3 = 4-MeSC6H4, 3,4,5-(MeO)3C6H2, 2,4-(Cl)2C6H3, 4-PhSO2C6H4, 2-MeSO2C6H4, 4-MeSO2C6H4, 4-PhSOC6H4, 2-MeSOC6H4, 4-MeSOC6H4, 2-PhCONHC6H4, 2-AcNHC6H4, 2-PhOC6H4, 4-PhSC6H4, 2-MeSC6H4; R4 = H, C6H5, 2,3-(Cl)2C6H3] are prepd. as nitrogen monoxide synthase inhibitors effective as pain killer and treatment or prevention of septicemia, endotoxin shock, chronic arthrorheumatism (no data). Thus, the title compd. I (R1 = C6H5CH2; R2 = H; R3 = 3,4,5-(MeO)3C6H2; R4 = H) was prepd.

L10 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2003 ACS
AN 1996:680346 CAPLUS
DN 126:8203
TI New antiinflammatory/antiarthritic heterocyclic bisphosphonates
AU Nugent, Richard A.; Dunn, Colin J.; Staite, Nigel D.; Murphy, Michael J.; Schlachter, Stephen T.; Aspar, Danielle G.; Shields, Sharon K.; Galinet, Louise A.
CS Upjohn Co., Kalamazoo, MI, 49001, USA
SO Phosphorus, Sulfur and Silicon and the Related Elements (**1996**), 109-110(1-4, Proceedings of the Thirteenth International Conference on Phosphorus Chemistry, 1995), 229-232
CODEN: PSSLEC; ISSN: 1042-6507
PB Gordon & Breach

DT Journal
LA English
AB In research toward a safe and effective treatment for **rheumatoid arthritis**, the authors identified new pyrazolo[**1**, **5**-a]**pyrimidine** and 4-pyrimidinone bisphosphonate esters, e.g., I and II, which are potent inhibitors of a murine model of chronic, cutaneous inflammation (delayed type hypersensitivity granuloma) and a murine antigen induced arthritis model. II has EC30 values of 0.01 and 0.005 mg/kg resp. and represents a new class of antiinflammatory/antiarthritic bisphosphonate ester.

L10 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2003 ACS
AN 1962:456311 CAPLUS
DN 57:56311
OREF 57:11209f-i,11210a
TI 3-Amino-s-triazolo[4,3-c] pyrimidines
IN Miller, George W.; Rose, Francis L.
PA Imperial Chemical Industries Ltd.
SO 10 pp.
DT Patent
LA Unavailable

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 898408		19620606	GB	19600226 <--

AB The title compds. were prepd. by the reaction of CNCl with 6-hydrazinopyrimidine derivs. under weakly acid, alk., or neutral conditions. Thus, 6-hydrazino-4-methyl-2-propylpyrimidine 5 in H2O 50 and EtOH 12 was treated with anhyd. Na2CO3 6 then with CNCl at 12-15.degree., with uptake of gas 2 parts, to give 3-amino-5-propyl-7-methyl-s-triazolo [4,3-c]pyrimidine, m. 240.degree.. 3-Amino-s-triazolo-[4,3-c]pyrimidines similarly prepd. were (other substituents and m.p. given): 5,7-dipropyl, 210-11.degree.; 5,7,8-trimethyl, 250.degree. (decompn.); 5,7-dimethyl, 250.degree. (decompn.); 7-butyl-5-propyl, 220-1.degree.; 5-tert-butyl-7-methyl, 202-4.degree.; 5-propyl-7-trifluoromethyl, 184.degree.; 5-ethyl-7-propyl, 220.degree.; 7-n-heptyl-5-propyl, 200.degree.; 7-methyl-5-pentyl, 219.degree.; 8-allyl-7-methyl-5-propyl, 170-2.degree.; 7-methyl-5,8-dipropyl, 169-70.degree.; 5,7-diethyl, 187.degree.; 5-ethyl-7-methyl, 225.degree. 4-Chloro-6-hydrazino-2-methylpyrimidine 10 in 20% aq. HOAc 250 contg. NaOAc 40 was treated with CNCl (uptake of 4.2 parts) to give 3-amino-5-methyl-7-chloro-s-triazolo-[4,3-c]pyrimidine, m. 190-5.degree. (decompn.). Similarly prepd. from 6-hydrazino-4-methyl-2-methylthiopyrimidine was 3-amino-5-methylthio-7-methyl-s-triazolo[4,3-c]pyrimidine, m. 232-4.degree. (decompn.), and from 2-ethylthio-6-hydrazino-4-methylpyrimidine was prepd. 3-amino-5-ethylthio-7-methyl-s-triazolo[4,3-c]pyrimidine, m. 209.degree.. 2-Amino-4-hy-drazino-6-methylpyrimidine 2.8 in H2O 15, 5N HOAc 4, and EtOH 5 was treated with NaOAc.3H2O 7, chilled to below 25.degree., and treated with CNCl (uptake parts) to 1.4 give 3,5-diamino-7-methyl-s-triazolo[4,3-c]pyrimidine, m. 203.degree. and 235.degree.. The title compds. were bronchodilators and respiratory stimulants. They also inhibited formation of granulomata and were useful in the treatment of **rheumatoid arthritis**. Cf. following abstr.

L10 ANSWER 6 OF 25 IFIPAT COPYRIGHT 2003 IFI
AN 3827428 IFIPAT;IFIUDB;IFICDB
TI PROTEASE INHIBITORS
INF Bondinell; William Edward, Wayne, PA
DesJarlais; Renee Louise, St. Davids, PA
Veber; Daniel Frank, Ambler, PA
Yamashita; Dennis Shinji, King of Prussia, PA
IN Bondinell William Edward; DesJarlais Renee Louise; Veber Daniel Frank; Yamashita Dennis Shinji

PAF SmithKline Beecham Corporation, Philadelphia, PA, US
PA Smithkline Beecham Corp (23499)
EXNAM Seaman, D Margaret
AG Hall Linda E.
Kinzig Charles M.
Venetianer Stephen
PI US 6518267 20030211
WO 9959526 19991125
AI US 2000-700828 20001121
WO 1999-US11266 19990520
20001121 PCT 371 date
20001121 PCT 102(e) date
PRAI US 1998-86557P 19980521 (Provisional)
FI US 6518267 20030211
DT Utility
FS CHEMICAL
GRANTED
CLMN 25
AB The present invention provides bis-aminomethyl carbonyl protease inhibitors and pharmaceutically acceptable salts, hydrates and solvates thereof which inhibit proteases, including cathepsin K, pharmaceutical compositions of such compounds, and methods for treating diseases of excessive bone loss or cartilage or matrix degradation, including osteoporosis; gingival disease including gingivitis and periodontitis; arthritis, more specifically, osteoarthritis and **rheumatoid arthritis**; Paget's disease; hypercalcemia of malignancy; and metabolic bone disease, comprising inhibiting said bone loss or excessive cartilage or matrix degradation by administering to a patient in need thereof a compound of the present invention.

L10 ANSWER 7 OF 25 IFIPAT COPYRIGHT 2003 IFI
AN 3674388 IFIPAT;IFIUDB;IFICDB
TI ANGIOGENESIS INHIBITORS; PYRAZOLO(**1,5**-A) **PYRIMIDINE** DERIVATIVES; TREATMENT OF TYROSINE KINASE-DEPENDENT DISEASES/CONDITIONS SUCH AS ANGIOGENESIS, CANCER, ATHEROSCLEROSIS, DIABETIC RETINOPATHY OR AUTOIMMUNE DISEASES
INF Bilodeau; Mark T., Lansdale, PA
Fraley; Mark E., North Wales, PA
Hungate; Randall W., Lansdale, PA
Kendall; Richard L., Thousand Oaks, CA
Rubino; Robert, Williamsville, NY
Rutledge; Ruth, Audubon, PA
Thomas Jr.; Kenneth A., Chatham, NJ
IN Bilodeau Mark T; Fraley Mark E; Hungate Randall W; Kendall Richard L; Rubino Robert; Rutledge Ruth; Thomas Kenneth A Jr
PAF Merck & Co., Inc., Rahway, NJ
PA Merck & Co Inc (54136)
EXNAM Jones, Dwayne C
AG Daniel, Mark R.
Garcia-Riva, J. Antonio
PI US 6380203 20020430
WO 9854093 19981203
AI US 1999-424132 19991118
WO 1998-US10590 19980526
19991118 PCT 371 date
19991118 PCT 102(e) date
XPD 26 May 2018
PRAI GB 1998-681 19980114
FI US 6380203 20020430
DT UTILITY
FS CHEMICAL
GRANTED

CLMN 14
AB The present invention relates to compounds which inhibit tyrosine kinase enzymes, compositions which contain tyrosine kinase inhibiting compounds and methods of using tyrosine kinase inhibitors to treat tyrosine kinase-dependent diseases/conditions such as angiogenesis, cancer, atherosclerosis, diabetic retinopathy or autoimmune diseases, in mammals.

L10 ANSWER 8 OF 25 IFIPAT COPYRIGHT 2003 IFI
AN 2031036 IFIPAT;IFIUDB;IFICDB
TI TRICYCLIC FUSED PRYIMIDINE DERIVATIVES, AND THEIR USE AS PHARMACEUTICALS; CONTAINING KETONE GROUP IN POSITION 2 AND 4 OF RING
INF Naka, Takehiko, Hyogo, JP
Saijo, Taketoshi, Hyogo, JP
Satoh, Hiroshi, Osaka, JP
IN Naka Takehiko (JP); Saijo Taketoshi (JP); Satoh Hiroshi (JP)
PAF Takeda Chemical Industries, Ltd, Osaka, JP
PA Takeda Chemical Industries Ltd JP (82624)
EXNAM Shah, Mukund J
EXNAM Rivers, Diana G
AG Wegner & Bretschneider
PI US 4912104 19900327 (CITED IN 001 LATER PATENTS)
AI US 1988-233080 19880816
XPD 16 Aug 2008
PRAI JP 1987-218964 19870831
JP 1988-130969 19880527
FI US 4912104 19900327
DT UTILITY; EXPIRED; CERTIFICATE OF CORRECTION
CDAT 22 Oct 1991
25 Feb 1992
FS CHEMICAL
GRANTED
MRN 004931 MFN: 0187
CLMN 22
AB Novel tricyclic fused pyrimidine derivatives represented by the formula (I):

D R A W I N G

wherein R1 and R2 are independently C1-8 alkyl or C2-8 alkenyl; R3 is hydrogen, C1-3 alkyl, C2-3 alkenyl, C1-6 alkyl-CO-, optionally substituted benzoyl, C1-4 alkyl-O-CO-, carbamoyl or formyl; and A is C2-4 alkylene or C2-4 alkenylene which may be substituted with C1-3 alkyl, halogen, nitro, amino, oxo, or phenyl optionally substituted with 1 to 2 members selected from the class consisting of amino, nitro, hydroxy, methoxy and methyl, and a salt thereof are useful for antiinflammatory, analgesic, antipyretic, antiallergic anti-psoriatic and liver-protecting agent.

L10 ANSWER 9 OF 25 SCISEARCH COPYRIGHT 2003 THOMSON ISI
AN 96:812779 SCISEARCH
GA The Genuine Article (R) Number: VQ054
TI NEW ANTI-INFLAMMATORY/ANTI-ARTHRITIC HETEROCYCLIC BISPHOSPHONATES
AU NUGENT R A (Reprint); DUNN C J; STAITE N D; MURPHY M J; SCHLACHTER S T; ASPAR D G; SHIELDS S K; GALINET L A
CS UPJOHN CO, KALAMAZOO, MI, 49001 (Reprint)
CYA USA
SO PHOSPHORUS SULFUR AND SILICON AND THE RELATED ELEMENTS, (**1996**) Vol. 110, No. 1-4, pp. 229-232.
ISSN: 0308-664X.
DT Article; Journal
LA ENGLISH
REC Reference Count: 8

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In the course of research toward a safe and effective treatment for **rheumatoid arthritis**, we identified new pyrazolo[**1,5-a**]**pyrimidine** and 4-pyrimidinone bisphosphonate esters, which are potent inhibitors of a murine model of chronic, cutaneous inflammation (delayed type hypersensitivity granuloma) and a murine antigen induced arthritis model. 9a has EC(30) values of 0.01 and 0.005 mg/kg respectively and represents a new class of antiinflammatory/antiarthritic bisphosphonate eater.

L10 ANSWER 10 OF 25 TOXCENTER COPYRIGHT 2003 ACS
AN 1999:210392 TOXCENTER
CP Copyright 2003 ACS
DN CA13202012322P
TI Preparation of pyrazolo[**1,5-a**]**pyrimidine** derivatives as nitrogen monoxide synthase inhibitors
AU Okamura, Takashi; Shoji, Yasuo; Shibutani, Tadao; Yasuda, Tsuneo; Iwamoto, Takeshi
CS ASSIGNEE: Otsuka Pharmaceutical Factory, Inc.
PI WO 9959998 A1 **25 Nov 1999**
SO (**1999**) PCT Int. Appl., 109 pp.
CODEN: PIXXD2.
CY JAPAN
DT Patent
FS CAPLUS
OS CAPLUS 1999:753238
LA Japanese
ED Entered STN: 20011116
Last Updated on STN: 20020403

AB Pyrazolo[**1,5-a**]**pyrimidine** derivs. represented by general formula [I; R1 = lower alkyl, Ph, thienyl; one of R2 and R3 = H and the other = naphthyl, furyl, pyridyl, styryl, phenylethynyl, (un)substituted Ph; R4 = H, lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, CO2H, lower alkoxycarbonyl, et.], which have pharmacol. effects including analgesic effect and nitrogen monoxide synthase inhibitory effect and are useful as analgesic agents and remedies and preventives for sepsis, endotoxin shock, chronic **rheumatoid arthritis**, etc., are prepd. Thus, 1.0 g di-Et (5-n-butylpyrazolo[1,5-a]pyrimidin-7-yl)methylphosphonate and 0.66 g 3,4,5-trimethoxybenzaldehyde were dissolved in 5.0 mL ethanol, cooled to 0.degree., treated with 3.8 mL 5% aq. NaOH, and stirred at 0.degree. for 1 h to give the title compd. (I; R1 = n-Bu, R2 = R4 = H, R3 = 3,4,5-trimethoxyphenyl) (II). In an analgesic assay against pressure-stimulated pain, II in vivo showed 47.8% recovery ratio of pain threshold value in the rear sole of rat in 60 min after the treatment with substance P. Pharmaceutical formulation contg. I were also prepd.

L10 ANSWER 11 OF 25 USPATFULL
AN 2003:40684 USPATFULL
TI Protease inhibitors
IN Bondinell, William Edward, Wayne, PA, United States
DesJarlais, Renee Louise, St. Davids, PA, United States
Veber, Daniel Frank, Ambler, PA, United States
Yamashita, Dennis Shinji, King of Prussia, PA, United States
PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 6518267 B1 20030211
WO 9959526 19991125 <--
AI US 2000-700828 20001121 (9)
WO 1999-US11266 19990520
PRAI US 1998-86557P 19980521 (60)
DT Utility

FS GRANTED
EXNAM Primary Examiner: Seaman, D. Margaret
LREP Hall, Linda E., Venetianer, Stephen, Kinzig, Charles M.
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 3549
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides bis-aminomethyl carbonyl protease inhibitors and pharmaceutically acceptable salts, hydrates and solvates thereof which inhibit proteases, including cathepsin K, pharmaceutical compositions of such compounds, and methods for treating diseases of excessive bone loss or cartilage or matrix degradation, including osteoporosis; gingival disease including gingivitis and periodontitis; arthritis, more specifically, osteoarthritis and **rheumatoid arthritis**; Paget's disease; hypercalcemia of malignancy; and metabolic bone disease, comprising inhibiting said bone loss or excessive cartilage or matrix degradation by administering to a patient in need thereof a compound of the present invention.

L10 ANSWER 12 OF 25 USPATFULL
AN 2003:20244 USPATFULL
TI 1,5-Diaryl substituted pyrazoles as p38 kinase inhibitors
IN Weier, Richard M., Lake Bluff, IL, United States
Crich, Joyce Z., Glenview, IL, United States
Xu, Xiang Dong, Gurnee, IL, United States
Collins, Paul W., Deerfield, IL, United States
PA Pharmacia Corporation, Saint Louis, MO, United States (U.S. corporation)
PI US 6509361 B1 20030121
WO 9958523 19991118 <--
AI US 2001-674653 20010212 (9)
WO 1999-US7036 19990512
20010212 PCT 371 date
DT Utility
FS GRANTED
EXNAM Primary Examiner: Aulakh, C. S.
LREP Gryte, Esq., David M., Harness, Dickey & Pierce, P.L.C.
CLMN Number of Claims: 57
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 3152
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention contemplates 1,5-diaryl-substituted pyrazole compounds that, inter alia, inhibit the activity of p38 MAP kinase. Also contemplated by the invention are processes for the preparation of the contemplated compounds and for the use of a contemplated compound in treating a mammalian host having a p38 kinase- or TNF-mediated disease.

L10 ANSWER 13 OF 25 USPATFULL
AN 2002:95800 USPATFULL
TI Angiogenesis inhibitors
IN Bilodeau, Mark T., Lansdale, PA, United States
Fraley, Mark E., North Wales, PA, United States
Hungate, Randall W., Lansdale, PA, United States
Kendall, Richard L., Thousand Oaks, CA, United States
Rutledge, Ruth, Audubon, PA, United States
Thomas, Jr., Kenneth A., Chatham, NJ, United States
Rubino, Robert, Williamsville, NY, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 6380203 B1 20020430
WO 9854093 19981203 <--
AI US 1999-424132 19991118 (9)

WO 1998-US10590 19980526
19991118 PCT 371 date
PRAI GB 1998-681 19980114
DT Utility
FS GRANTED
EXNAM Primary Examiner: Jones, Dwayne C.
LREP Garcia-Riva, J. Antonio, Daniel, Mark R.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 870
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compounds which inhibit tyrosine kinase enzymes, compositions which contain tyrosine kinase inhibiting compounds and methods of using tyrosine kinase inhibitors to treat tyrosine kinase-dependent diseases/conditions such as angiogenesis, cancer, atherosclerosis, diabetic retinopathy or autoimmune diseases, in mammals.

L10 ANSWER 14 OF 25 USPATFULL
AN 2000:7079 USPATFULL
TI Trapidil for use in the therapy of syndrome that may be influenced by immunomodulators
IN Walch, Hatto, Laupheim, Germany, Federal Republic of
PA Rodleben Pharma GmbH, Rodleben, Germany, Federal Republic of (non-U.S. corporation)
PI US 6015578 20000118
WO 9632111 19961017 <--
AI US 1997-945216 19971009 (8)
WO 1996-EP1037 19960311
19971009 PCT 371 date
19971009 PCT 102(e) date
PRAI DE 1995-19514048 19950413
DT Utility
FS Granted
EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Benston, Jr., William Edward
LREP Ratner & Prestia
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 395
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Trapidil is used in the therapy of syndromes that may be influenced by immunomodulators. Trapidil is used for the preparation of a drug for the therapy or prophylaxis of diseases associated with TNF-induced pathological disorders.

L10 ANSWER 15 OF 25 USPATFULL
AN 97:56661 USPATFULL
TI Phosphonoacetic esters and acids as anti-inflammatories
IN Nugent, Richard A., Galesburg, MI, United States
Anderson, David J., Kalamazoo, MI, United States
Schlachter, Stephen T., Kalamazoo, MI, United States
PA The Upjohn Company, Kalamazoo, MI, United States (U.S. corporation)
PI US 5643895 19970701 <--
AI US 1996-654801 19960529 (8)
RLI Division of Ser. No. US 1995-382240, filed on 1 Feb 1995, now patented, Pat. No. US 5565641 which is a continuation of Ser. No. US 1992-926879, filed on 7 Aug 1992, now abandoned
DT Utility
FS Granted

EXNAM Primary Examiner: Berch, Mark L.; Assistant Examiner: Kifle, Brock
LREP Corneglio, Donald L.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 520
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds useful in the treatment of inflammation structurally represented as Formula I ##STR1## one of X or Y is H and the other is selected from the group consisting of: ##STR2## or X and Y are taken together to form a ring selected from the group consisting of: ##STR3## as herein defined. The compounds are useful as anti-inflammatory and anti-arthritic agents.

L10 ANSWER 16 OF 25 USPATFULL
AN 97:47400 USPATFULL
TI Pyrimidine bisphosphonate esters and (alkoxymethylphosphinyl)alkyl phosphonic acids as anti-inflammatories
IN White, David R., Kalamazoo, MI, United States
Fritzen, Jr., Edward L., Kalamazoo, MI, United States
PA The Upjohn Company, Kalamazoo, MI, United States (U.S. corporation)
PI US 5635495 19970603 <--
WO 9409017 19940428 <--
AI US 1995-416797 19950406 (8)
WO 1993-US8626 19930920
19950406 PCT 371 date
19950406 PCT 102(e) date
RLI Continuation-in-part of Ser. No. US 1992-959316, filed on 9 Oct 1992, now abandoned And Ser. No. US 1992-958986, filed on 9 Oct 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Bernhardt, Emily
LREP Corneglio, Donald L.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 997
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds useful in the treatment of inflammation structurally represented as ##STR1## wherein X,X.sup.1 and R groups are as herein defined.

L10 ANSWER 17 OF 25 USPATFULL
AN 97:36191 USPATFULL
TI Pyrazole derivatives
IN Oku, Teruo, Tsukuba, Japan
Kawai, Yoshio, Ushiku, Japan
Marusawa, Hiroshi, Yokohama, Japan
Yamazaki, Hitoshi, Tsukuba, Japan
Abe, Yoshito, Tsukuba, Japan
PA Fujisawa Pharmaceutical Co., Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5624931 19970429 <--
AI US 1995-471175 19950606 (8)
RLI Division of Ser. No. US 1994-269520, filed on 1 Jul 1994, now patented, Pat. No. US 5478827 which is a division of Ser. No. US 1992-931093, filed on 17 Aug 1992, now patented, Pat. No. US 5356897
PRAI GB 1991-19267 19910909
GB 1992-4464 19920302
DT Utility
FS Granted
EXNAM Primary Examiner: Gupta, Yogendra N.

LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2216
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Pyrazole derivatives useful for inhibiting the production of Interleukin-1 (IL-1) and tumor necrosis factor (TNF) and the like, which can be represented by the following formula: ##STR1## and a pharmaceutical composition containing the same and to uses thereof.

L10 ANSWER 18 OF 25 USPATFULL
AN 96:94571 USPATFULL
TI Phosphonoacetic esters and acids as anti-inflammatories
IN Nugent, Richard A., Galesburg, MI, United States
Anderson, David J., Kalamazoo, MI, United States
Schlachter, Stephen T., Kalamazoo, MI, United States
PA The Upjohn Company, Kalamazoo, MI, United States (U.S. corporation)
PI US 5565441 19961015 <--
AI US 1995-382240 19950201 (8)
RLI Continuation of Ser. No. US 1992-926879, filed on 7 Aug 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Berch, Mark L.
LREP Corneglio, Donald L.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 526
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds useful in the treatment of inflammation structurally represented as Formula I ##STR1## one of X or Y is H and the other is selected from the group consisting of: ##STR2## or X and Y are taken together to form a ring selected from the group consisting of: ##STR3## as herein defined. The compounds are useful as anti-inflammatory and anti-arthritic agents.

L10 ANSWER 19 OF 25 USPATFULL
AN 96:29562 USPATFULL
TI Desosamino derivatives of macrolides as immunosuppressants and antifungal agents
IN Hauske, James R., East Lyme, CT, United States
Schulte, Gary R., Stonington, CT, United States
PA Pfizer Inc., New York, NY, United States (U.S. corporation)
PI US 5506233 19960409 <--
WO 9318042 19930916 <--
AI US 1994-284526 19940808 (8)
WO 1993-US426 19930127
19940808 PCT 371 date
19940808 PCT 102(e) date
RLI Continuation of Ser. No. US 1992-844350, filed on 2 Mar 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Bond, Robert T.
LREP Richardson, Peter C., Benson, Gregg C., Ronau, Robert T.
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2110
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Macrolides of the FK-506 type and methods of treatment of resistance to transplantation, fungal infections, and autoimmune diseases such as **rheumatoid arthritis** and psoriasis using said macrolides.

L10 ANSWER 20 OF 25 USPATFULL
AN 95:114741 USPATFULL
TI Pyrazole derivatives
IN Oku, Teruo, Tsukuba, Japan
Kawai, Yoshio, Ushiku, Japan
Marusawa, Hiroshi, Yokohama, Japan
Yamazaki, Hitoshi, Tsukuba, Japan
Abe, Yoshito, Tsukuba, Japan
Tanaka, Hirokazu, Tsuchiura, Japan
PA Fujisawa Pharmaceutical Co., Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5478827 19951226 <--
AI US 1994-269520 19940701 (8)
RLI Division of Ser. No. US 1992-931093, filed on 17 Aug 1992, now patented, Pat. No. US 5356897
PRAI GB 1991-19267 19910909
GB 1992-4464 19920302
DT Utility
FS Granted
EXNAM Primary Examiner: Gupta, Yogendra N.
LREP Oblon, Spivak, McClelland, Maier & Neustadt
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2161
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to heterocyclic derivatives useful for inhibiting the production of Interleukin-1 (IL-1) and tumor necrosis factor (TNF) and the like, which can be represented by the following formula: ##STR1## to a process for their production, to a pharmaceutical composition containing the same and to uses thereof.

L10 ANSWER 21 OF 25 USPATFULL
AN 95:22896 USPATFULL
TI Pyrazolopyrimidine and pyrimidinyl bisphosphonic esters as anti-inflammatories
IN Nugent, Richard A., Galesburg, MI, United States
Schlachter, Stephen T., Kalamazoo, MI, United States
PA The Upjohn Company, Kalamazoo, MI, United States (U.S. corporation)
PI US 5397774 19950314 <--
AI US 1993-175216 19931228 (8)
RLI Continuation-in-part of Ser. No. US 1991-725047, filed on 3 Jul 1991, now abandoned And a continuation-in-part of Ser. No. US 1991-725046, filed on 3 Jul 1991, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Bernhardt, Emily
LREP Corneglio, Donald
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 747
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds useful in the treatment of inflammation structurally represented as ##STR1## wherein X is O or S and the R groups are as herein defined. The compounds are useful as anti-inflammatory and anti-arthritic agents without inhibiting prostaglandin synthesis.

L10 ANSWER 22 OF 25 USPATFULL
AN 94:102233 USPATFULL
TI Amidine group containing monocycloheteracyclic or bicycloheterocyclic diphosphonic acid derivatives and medicaments containing these compounds
IN Bosies, Elmar, Weinheim, Germany, Federal Republic of
Zilch, Harald, Mannheim, Germany, Federal Republic of
PA Boehringer Mannheim GmbH, Mannheim, Germany, Federal Republic of (non-U.S. corporation)
PI US 5366969 19941122 <--
AI US 1992-829019 19920306 (7)
PRAI DE 1989-3930130 19890909
DT Utility
FS Granted
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Sripada, P. K.
LREP Nikaido Marmelstein Murray & Oram
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 381
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the formula I ##STR1## in which R can be hydrogen or C.sub.1 -C.sub.4 -alkyl, R.sup.1 hydrogen, C.sub.1 -C.sub.6 -alkyl, aryl, aryl-C.sub.1 -C.sub.4 -alkyl, amino-C.sub.1 -C.sub.6 -alkyl, C.sub.1 -C.sub.6 -alkylamino-C.sub.1 -C.sub.4 -alkyl, C.sub.1 -C.sub.6 -dialkylamino-C.sub.1 -C.sub.4 -alkyl, C.sub.1 -C.sub.4 -alkoxy-C.sub.1 -C.sub.4 -alkyl, C.sub.1 -C.sub.4 -alkylthio-C.sub.1 -C.sub.4 -alkyl, C.sub.3 -C.sub.7 -alkenyl, R.sup.2 R.sup.1 or C.sub.2 -C.sub.7 -alkenyl, C.sub.1 -C.sub.6 -alkylmercapto, C.sub.1 -C.sub.6 -alkoxy, phenoxy-C.sub.1 -C.sub.4 -alkyl,amino, C.sub.1 -C.sub.4 -alkylamino, di-C.sub.1 -C.sub.4 -alkylamino, morpholino, thiomorpholino, pyrrolidino, piperidino, hexamethyleneimino, pyrasolino, imidazolino, n 0, 1 or 2 and R.sup.1 and R.sup.2, together with the carbon and the nitrogen atom to which they are attached, can form a heterocyclic five-, six- or seven-membered ring with 1-4 heteroatoms, whereby the heteroatoms can be the same or different and signify oxygen, nitrogen or sulphur and the annelated ring can possibly be substituted by one or more C.sub.1 -C.sub.6 -alkyl, C.sub.1 -C.sub.6 -alkoxy, C.sub.1 -C.sub.6 -alkylmercapto groups, hydroxyl, amino, nitro, halogen or halomethyl, as well as their pharmacologically acceptable salts, processes for their preparation, as well as medicaments which contain these compounds for the treatment of calcium metabolism disturbances.

L10 ANSWER 23 OF 25 USPATFULL
AN 94:91054 USPATFULL
TI 3-(heteroaryl)-pyrazololi[1,5-a]pyrimidines
IN Oku, Teruo, Tsukuba, Japan
Kawai, Yoshio, Ushiku, Japan
Marusawa, Hiroshi, Yokohama, Japan
Yamazaki, Hitoshi, Tsukuba, Japan
Abe, Yoshito, Tsukuba, Japan
Tanaka, Hirokazu, Tsuchiura, Japan
PA Fujisawa Pharmaceutical Co., Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5356897 19941018 <--
AI US 1992-931093 19920817 (7)
PRAI GB 1991-19267 19910909
GB 1992-4464 19920302
DT Utility
FS Granted
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Gupta, Y. N.
LREP Drehkoff, W. Dennis
CLMN Number of Claims: 8
ECL Exemplary Claim: 1

DRWN No Drawings
LN.CNT 2077
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to heterocyclic derivatives useful for inhibiting the production of Interleukin-1 (IL-1) and tumor necrosis factor (TNF) and the like, which can be represented by the following formula: ##STR1## to a process for their production, to a pharmaceutical composition containing the same and to uses thereof.

L10 ANSWER 24 OF 25 USPATFULL
AN 90:23604 USPATFULL
TI Tricyclic fused pryimidine derivatives, and their use as pharmaceuticals
IN Naka, Takehiko, Hyogo, Japan
Saijo, Taketoshi, Hyogo, Japan
Satoh, Hiroshi, Osaka, Japan
PA Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 4912104 19900327 <--
AI US 1988-233080 19880816 (7)
PRAI JP 1987-218964 19870831
JP 1988-130969 19880527
DT Utility
FS Granted
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Rivers, Diana G.
LREP Wegner & Bretschneider
CLMN Number of Claims: 22
ECL Exemplary Claim: 1,19
DRWN No Drawings
LN.CNT 1962
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel tricyclic fused pyrimidine derivatives represented by the formula (I): ##STR1## wherein R.sup.1 and R.sup.2 are independently C.sub.1-8 alkyl or C.sub.2-8 alkenyl;

R.sup.3 is hydrogen, C.sub.1-3 alkyl, C.sub.2-3 alkenyl, C.sub.1-6 alkyl-CO-, optionally substituted benzoyl, C.sub.1-4 alkyl-O-CO-, carbamoyl or formyl; and

A is C.sub.2-4 alkylene or C.sub.2-4 alkenylene which may be substituted with C.sub.1-3 alkyl, halogen, nitro, amino, oxo, or phenyl optionally substituted with 1 to 2 members selected from the class consisting of amino, nitro, hydroxy, methoxy and methyl, and a salt thereof

are useful for antiinflammatory, analgesic, antipyretic, anti-allergic anti-psoriatic and liver-protecting agent.

L10 ANSWER 25 OF 25 USPATFULL
AN 84:63733 USPATFULL
TI Substituted 1H-pyrazolo (1,5-a) pyrimidines and process for their preparation
IN Doria, Gianfederico, Milan, Italy
Passarotti, Carlo, Gallarate, Italy
Buttinoni, Ada, Milan, Italy
PA Farmitalia Carlo Erba S.p.A., Milan, Italy (non-U.S. corporation)
PI US 4482555 19841113 <--
AI US 1983-474205 19830310 (6)
PRAI GB 1982-7637 19820316
GB 1983-3089 19830204
DT Utility
FS Granted
EXNAM Primary Examiner: Gerstl, Robert; Assistant Examiner: Gibson, Sharon A.
LREP Murray, Whisenhunt and Ferguson
CLMN Number of Claims: 10

ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1798
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of general formula (I) ##STR1## wherein R.sub.1 is a 2-pyridyl, 3-pyridyl or 4-pyridyl group; (b) a phenyl ring, unsubstituted or substituted by one or two groups chosen from halogen, trihalo-C.sub.1 -C.sub.4 alkyl, C.sub.1 -C.sub.6 alkyl, nitro, amino and C.sub.2 -C.sub.6 alkanoylamino; (c) benzyl; or (d) C.sub.1 -C.sub.6 alkyl;

each of R.sub.2 and R.sub.3 independently is a hydrogen or a halogen atom or C.sub.1 -C.sub.6 alkyl;

R.sub.4 is hydrogen, C.sub.1 -C.sub.6 alkyl or phenyl;

R.sub.5 is (a') ##STR2## wherein each of R.sub.6 and R.sub.7 independently is hydrogen or C.sub.1 -C.sub.6 alkyl, or R.sub.6 and R.sub.7, taken together with the nitrogen atom to which they are linked, form a morpholino, piperidino, N-pyrrolidinyl or N-piperazinyl ring, wherein the N-piperazinyl ring is unsubstituted or substituted by C.sub.1 -C.sub.6 alkyl;

(b') a ##STR3## wherein R.sub.8 is hydrogen, C.sub.1 -C.sub.4 alkyl, C.sub.1 -C.sub.4 alkoxy or halogen;

(c') --NHR.sub.9, wherein R.sub.9 is a 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrimidinyl, 2-pyrazinyl, 3-pyrazolyl, 2-thiazolyl or 2-benzothiazolyl group, each of these groups being unsubstituted or substituted by one or two groups chosen from halogen, C.sub.1 -C.sub.6 alkyl, phenyl, hydroxy and C.sub.1 -C.sub.6 alkoxy;

(d') ##STR4## wherein m is 1, 2 or 3 and R.sub.6 and R.sub.7 are as defined above; or the pharmaceutically acceptable salts thereof; are disclosed as anti-inflammatory agents.

=> d l10 1-25 kwic

L10 ANSWER 1 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI PYRAZOLO-**1 5**-A-**PYRIMIDINE** DERIVATIVES AS POTENTIAL ANTIARTHRITIC AGENTS.
SO THIRD CHEMICAL CONGRESS OF NORTH AMERICA HELD AT THE 195TH AMERICAN CHEMICAL SOCIETY MEETING, TORONTO, ONTARIO, CANADA, JUNE 5-10, 1988. ABSTR PAP CHEM CONGR NORTH AM. (1988) 3 (2), MEDI 139.
CODEN: ABPAEK.
IT Miscellaneous Descriptors
ABSTRACT STRUCTURE-ACTIVITY RELATIONSHIP ANTIARTHRITIC-DRUG U-76670 3 CYANO-2 5 7-TRIMETHYLPYRAZOLO-**1 5**-A-**PYRIMIDINE RHEUMATOID ARTHRITIS**

L10 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2003 ACS
TI Preparation of pyrazolo[**1,5**-a]**pyrimidine** derivatives as nitrogen monoxide synthase inhibitors
PI WO 9959998 A1 **19991125**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9959998	A1	19991125	WO 1999-JP2572	19990517 <--
W: AU, CA, CN, JP, KR, NO, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2331468	AA	19991125	CA 1999-2331468	19990517 <--

AU 9937320	A1	19991206	AU 1999-37320	19990517 <--	
AU 751337	B2	20020815			
EP 1081149	A1	20010307	EP 1999-919634	19990517	
EP 1081149	B1	20030402			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AT 236166	E	20030415	AT 1999-919634	19990517	
NO 2000005820	A	20001117	NO 2000-5820	20001117	
US 6372749	B1	20020416	US 2000-700764	20001120	

AB Pyrazolo[**1,5**-a]**pyrimidine** derivs. represented by general formula [I; R1 = lower alkyl, Ph, thienyl; one of R2 and R3 = H and. . . nitrogen monoxide synthase inhibitory effect and are useful as analgesic agents and remedies and preventives for sepsis, endotoxin shock, chronic **rheumatoid arthritis**, etc., are prepd. Thus, 1.0 g di-Et (5-n-butylpyrazolo[1,5-a]pyrimidin-7-yl)methylphosphonate and 0.66 g 3,4,5-trimethoxybenzaldehyde were dissolved in 5.0 mL ethanol, cooled to. . .

IT **Rheumatoid arthritis**
(chronic; prepn. of pyrazolo[**1,5**-a]**pyrimidine** derivs. as nitrogen monoxide synthase inhibitors and analgesics and for treatment and prevention of endotoxin shock, and chronic **rheumatoid arthritis**)

IT Analgesics
Sepsis
(prepn. of pyrazolo[**1,5**-a]**pyrimidine** derivs. as nitrogen monoxide synthase inhibitors and analgesics and for treatment and prevention of endotoxin shock, and chronic **rheumatoid arthritis**)

IT Shock (circulatory collapse)
(septic; prepn. of pyrazolo[**1,5**-a]**pyrimidine** derivs. as nitrogen monoxide synthase inhibitors and analgesics and for treatment and prevention of endotoxin shock, and chronic **rheumatoid arthritis**)

IT

251363-62-9P	251363-63-0P	251363-64-1P	251363-65-2P	251363-66-3P
251363-67-4P	251363-68-5P	251363-69-6P	251363-70-9P	251363-71-0P
251363-72-1P	251363-73-2P	251363-74-3P	251363-75-4P	251363-76-5P
251363-77-6P	251363-78-7P	251363-79-8P	251363-80-1P	251363-81-2P
251363-82-3P	251363-83-4P	251363-84-5P	251363-85-6P	251363-86-7P
251363-87-8P	251363-88-9P	251363-89-0P	251363-90-3P	251363-91-4P
251363-92-5P	251363-94-7P	251363-95-8P	251363-96-9P	251363-97-0P
251363-98-1P	251363-99-2P	251364-00-8P	251364-01-9P	251364-02-0P
251364-03-1P	251364-04-2P	251364-05-3P	251364-06-4P	251364-07-5P
251364-08-6P	251364-09-7P	251364-10-0P	251364-11-1P	251364-12-2P
251364-13-3P	251364-14-4P	251364-15-5P	251364-16-6P	251364-17-7P
251364-18-8P	251364-19-9P	251364-20-2P	251364-21-3P	251364-22-4P
251364-23-5P	251364-24-6P	251364-25-7P	251364-26-8P	251364-27-9P
251364-28-0P	251364-29-1P	251364-30-4P	251364-31-5P	251364-32-6P
251364-33-7P	251364-34-8P	251364-35-9P	251364-36-0P	251364-37-1P
251364-38-2P	251364-39-3P	251364-40-6P	251364-41-7P	251364-42-8P
251364-43-9P	251364-44-0P	251364-45-1P	251364-46-2P	251364-47-3P
251364-48-4P	251364-49-5P	251364-50-8P	251364-51-9P	251364-52-0P
251364-53-1P	251364-54-2P	251364-55-3P	251364-56-4P	251364-57-5P
251364-58-6P	251364-59-7P	251364-60-0P	251364-61-1P	251364-62-2P
251364-63-3P	251364-64-4P	251364-65-5P	251364-66-6P	251364-67-7P
251364-68-8P	251364-69-9P	251364-70-2P	251364-71-3P	

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrazolo[**1,5**-a]**pyrimidine** derivs. as nitrogen monoxide synthase inhibitors and analgesics and for treatment and prevention of endotoxin shock, and chronic **rheumatoid arthritis**)

IT 125978-95-2, Nitric oxide synthase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of pyrazolo[**1,5**-a]**pyrimidine** derivs. as nitrogen monoxide synthase inhibitors and analgesics and for treatment and prevention of endotoxin shock, and chronic **rheumatoid arthritis**)

IT 75-03-6, Ethyl iodide 75-04-7, Ethylamine, reactions 78-38-6, Diethyl ethylphosphonate 86-81-7, 3,4,5-Trimethoxybenzaldehyde 104-88-1, 4-Chlorobenzaldehyde, reactions 106-48-9, 4-Chlorophenol 108-98-5, Thiophenol, reactions 867-13-0, Triethyl phosphonoacetate 28460-01-7, Diethyl methylthiomethylphosphonate 57230-04-3, 3-Benzyloxy-4,5-dimethoxybenzaldehyde 59481-63-9 167371-63-3, 5-Butyl-7-chloropyrazolo[**1,5**-a]**pyrimidine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pyrazolo[**1,5**-a]**pyrimidine** derivs. as nitrogen monoxide synthase inhibitors and analgesics and for treatment and prevention of endotoxin shock, and chronic **rheumatoid arthritis**)

IT 251364-72-4P 251364-73-5P 251364-74-6P 251364-75-7P 251364-76-8P 251364-77-9P 251364-78-0P 251364-79-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of pyrazolo[**1,5**-a]**pyrimidine** derivs. as nitrogen monoxide synthase inhibitors and analgesics and for treatment and prevention of endotoxin shock, and chronic **rheumatoid arthritis**)

L10 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2003 ACS
PI JP 11279178 A2 **19991012** Heisei

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11279178	A2	19991012	JP 1999-18861	19990127 <--

IT Analgesics
Antirheumatic agents
Rheumatoid arthritis
Septicemia
(prepn. of pyrazolo[1,5-a]pyrimidines as nitrogen monoxide synthase inhibitors)

IT 167371-62-2P, 5-Butyl-7-hydroxypyrazolo[**1,5**-a]**pyrimidine** 167371-63-3P, 5-Butyl-7-chloropyrazolo[**1,5**-a]**pyrimidine** 174859-60-0P 245095-95-8P 245095-96-9P 245095-97-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of pyrazolo[1,5-a]pyrimidines as nitrogen monoxide synthase inhibitors)

L10 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2003 ACS
SO Phosphorus, Sulfur and Silicon and the Related Elements (**1996**), 109-110(1-4, Proceedings of the Thirteenth International Conference on Phosphorus Chemistry, 1995), 229-232
CODEN: PSSLEC; ISSN: 1042-6507
AB In research toward a safe and effective treatment for **rheumatoid arthritis**, the authors identified new pyrazolo[**1,5**-a]**pyrimidine** and 4-pyrimidinone bisphosphonate esters, e.g., I and II, which are potent inhibitors of a murine model of chronic, cutaneous inflammation. . .

L10 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2003 ACS
PI GB 898408 **19620606**

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	GB 898408	19620606	GB	19600226 <--	

AB . . . title compds. were bronchodilators and respiratory stimulants. They also inhibited formation of granulomata and were useful in the treatment of **rheumatoid arthritis**. Cf. following abstr.

IT s-Triazolo[**1**,**5**-c]**pyrimidine**, 2-amino-
s-Triazolo[4,3-c]pyrimidine, 3-amino-
(derivs.)

L10 ANSWER 6 OF 25 IFIPAT COPYRIGHT 2003 IFI

PI US 6518267 20030211
WO 9959526 19991125

AB . . . bone loss or cartilage or matrix degradation, including osteoporosis; gingival disease including gingivitis and periodontitis; arthritis, more specifically, osteoarthritis and **rheumatoid arthritis**; Paget's disease; hypercalcemia of malignancy; and metabolic bone disease, comprising inhibiting said bone loss or excessive cartilage or matrix degradation. . .

ECLM . . . phenyl, thiophene, benzthiazole, 2, 3, 4, 5, 6, or 7 quinoline, naphthyl, C0-C6alkyl pyrazole, Nmethyl pyrrole, and benzoxazole; pyrazine; pyrimidine; 2,7-dimethylpyrazolo(**1**,**5**-a) **pyrimidine** and 4,7-dimethylpyrazolo(5,1-c)(1,2,4)-triazine, R6 is selected from the group consisting of: phenyl and phenyl substituted with C0-C6 alkyl, N-piperidine, benzofuran; or. . .

ACLM . . . 1N-(N-(biphenyl)-4-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(indole-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl) -amino-propan-2-1N-(N-(indole-6-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl) -phenylacetyl)-amino-propan-2-one; 1N-(N-(adamantane-1-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl-amino-propan-2-one; 1N-(N-(1-methoxy-2-naphthoyl)-leucine)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(thieno(3,2-b)thiophene-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl) -phenylacetyl)-amino-propan-2-one; 1N-(N-(4-cyclohexylbenzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl) -amino-propan-2-one; 1N-(N-(1-methylpyrrole-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl) -phenyacetyl)-amino-propan-2-one; 1N-(N-(4-methoxybenzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl) -amino-propan-2-one; 1N-(N-(thiophene-3-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4-(4'-ethylbiphenyl)carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl) -phenylacetyl)-amino-propan-2-one; 1N-(N-(pyrazine-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl) -amino-propan-2-one; 1N-(N-(2,7-dimethylpyrazolo(**1**,**5**-a)**pyrimidine** -6-carbonyl)-leucinyl)-amino-3N -(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-1N-(N-(4,7-dimethylpyrazolo(5,1-c)(1,2,4)triazine-3-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl) -phenylacetyl)-amino-propan-2-1N-(N-thianaphthenyl-2-carbonyl)-leucinyl) -amino-3N-(3-(6-methyl-2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-thianaphthenyl-2-carbonyl)-leucinyl)-amino-3N-(3-(5-methyl-2-pyridyl) -phenylacetyl)-amino-propan-2-one; 1N-(N-(4-trifluoromethylbenzoyl)-leucinyl)-amino-3N-(3-(6-methyl-2-pyridyl) -phenylacetyl)-amino-propan-2-one; 1N-(N-(4-trifluoromethylbenzoyl)-leucinyl)-amino-3N-(3-(4-methyl-2-pyridyl) -phenylacetyl)-amino-propan-2-one; 1N-(N-(N-tert-butoxycarbonyl-leucinyl)-amino-3N-(3-(2-pyridyl) phenylacetyl)-amino-propan-2-one; 1N-(N-(4-((2-dimethylamino)ethoxy)-benzoyl)-leucinyl)-amino-3N-(3-(2 -pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-((2-dimethylamino)ethoxy)-3-methoxy-benzoyl)-leucinyl)-amino-3N-(3 -(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-(dimethylaminoethoxy)benzoyl)-leucinyl)-amino-3N-(3-(2 -pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-((2-

dimethylamino)ethoxy)-4-methoxy-benzoyl)-leucinyl)-amino-3N-(3
-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-((2-
(piperidinyl)ethoxy)4-methoxy-benzoyl)-leucinyl)-amino-3N-(3-(2-
pyridyl)phenylacetyl)-amino-propan-2-one;. . .
. . . 1N-(N-(adamantane-1-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)
-phenylacetyl)-amino-propan-2-one; 1N-(N-(1-methoxy-2-naphthoyl)-
leucinyl)-amino-3N-(3-(2-pyridyl) -phenylacetyl)-amino-propan-2-one;
1N-(N-(benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-
propan-2-one; 1N-(N-(thieno(3,2-b)thiophene-2-carbonyl)-leucinyl)-amino-
3N-(3-(2-pyridyl) -phenylacetyl)-amino-propan-2-one; 1N-(N-(4-
cyclohexylbenzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)
-amino-propan-2-one; 1N-(N-(1-methylpyrrole-2-carbonyl)-leucinyl)-amino-
3N-(3-(2-pyridyl) -phenylacetyl)-amino-propan-2-one; 1N-(N-(4-
methoxybenzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)
-amino-propan-2-one; 1N-(N-(thiophene-3-carbonyl)-leucinyl)-amino-3N-(3-
(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4-(4'-
ethylbiphenyl)carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)
-phenylacetyl)-amino-propan-2-one; 1N-(N-(pyrazine-2-carbonyl)-leucinyl)-
amino-3N-(3-(2-pyridyl)-phenylacetyl) -amino-propan-2-one;
1N-(N-(pyrimidine-4-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)
-phenylacetyl)-amino-propan-2-one; 1N-(N-(2,7-dimethylpyrazolo(**1**
, **5**-a)**pyrimidine**-6-carbonyl)-leucinyl)-amino-3N-(3-(2-
pyridyl)-phenylacetyl) -amino-propan-2-one; 1N-(N-(4,7-
dimethylpyrazolo(5,1-c)(1,2,4)triazine-3-carbonyl)-leucinyl)
-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-1N-(N-
thianaphthenyl-2-carbonyl)-leucinyl)-amino-3N-(3-(6-methyl-2-pyridyl)-
phenylacetyl)-amino -propan-2-one; 1N-(N-thianaphthenyl-2-carbonyl)-
leucinyl)-amino-3N-(3-(5-methyl-2-pyridyl) -phenylacetyl)-amino-propan-2-
one; 1N-(N-(4-trifluoromethylbenzoyl)-leucinyl)-amino-3N-(3-(6-methyl-2-
pyridyl) -phenylacetyl)-amino-propan-2-one; 1N-(N-(4-
trifluoromethylbenzoyl)-leucinyl)-amino-3N-(3-(4-methyl-2-pyridyl)
-phenylacetyl)-amino-propan-2-one; 1N-(N-tert-butoxycarbonyl-leucinyl)-
amino-3N-(4-nitrophenylmethoxycarbonyl) -amino-propan-2-one;
1N-(N-(4-((2-dimethylamino)ethoxy)-benzoyl)-leucinyl)-amino-3N-(3-(2
-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-((2-
dimethylamino)ethoxy)-3-methoxy-benzoyl)-leucinyl)-amino-3N-(3
-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-
(dimethylaminoethoxy)benzoyl)-leucinyl)-amino-3N-(3-(2
-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-((2-
dimethylamino)ethoxy)4-methoxy-benzoyl)-leucinyl)-amino-3N-(3
-(2-pyridyl)phenylacetyl)-amino-propan-2-one;. . .
18. A method according to claim 16 wherein said disease is
rheumatoid arthritis.
25. A method according to claim 23 wherein said disease is
rheumatoid arthritis.

L10 ANSWER 7 OF 25 IFIPAT COPYRIGHT 2003 IFI
TI ANGIOGENESIS INHIBITORS; PYRAZOLO(**1**,**5**-A)
PYRIMIDINE DERIVATIVES; TREATMENT OF TYROSINE KINASE-DEPENDENT
DISEASES/CONDITIONS SUCH AS ANGIOGENESIS, CANCER, ATHEROSCLEROSIS,
DIABETIC RETINOPATHY OR AUTOIMMUNE DISEASES
PI US 6380203 20020430
WO 9854093 19981203
ECLM 1. A compound in accordance with formula I:

2-R2,3-R1,5-R5,6-R4,7-R3-PYRAZOLO(**1**,**5**-a)
PYRIMIDINE I

or a pharmaceutically acceptable salt, hydrate or prodrug thereof,
wherein R1 is aryl, optionally substituted with one to three
substituents. . .
ACLM 2. A compound in accordance with claim 1 which is: 3-(4-fluorophenyl)-6-

(4-pyridyl) pyrazolo(1,5-A)**pyrimidine**,
3-(3-chlorophenyl)-6-(4-pyridyl) pyrazolo(1,5-A)
pyrimidine, 3-(3,4-methylenedioxyphenyl)-6-(4-pyridyl) pyrazolo(
1,5-A) **pyrimidine**, 3-(phenyl)-6-(4-pyrimidyl)
pyrazolo(1,5-A)**pyrimidine**,
3-(4-fluorophenyl)-6-(4-pyrimidyl) pyrazolo(1,5-A)
pyrimidine, 3-(3-chlorophenyl)-6-(4-pyrimidyl) pyrazolo(1
,5-A)**pyrimidine**, 3-(3-acetamidophenyl)-6-(4-
methylphenyl) pyrazolo(1,5-A) **pyrimidine**,
3-(phenyl)-6-(4-methoxyphenyl) pyrazolo(1,5-A)
pyrimidine, 3-(3-acetamidophenyl)-6-(4-methoxyphenyl)pyrazolo(
1,5-A) **pyrimidine**, 3-(phenyl)-6-(4-
methoxyphenyl) pyrazolo(1,5-A)**pyrimidine**,
3-(phenyl)-6-(4-chlorophenyl) pyrazolo(1,5-A)
pyrimidine, 3-(phenyl)-6-(4-methylphenyl) pyrazolo(1,
5-A)**pyrimidine**, 3-(phenyl)-6-(2-pyridyl) pyrazolo(
1,5-A)**pyrimidine**, 3-(phenyl)-6-(4-pyrimidyl)
pyrazolo(1,5-A)**pyrimidine**,
3-(phenyl)-6-(2-pyrazinyl) pyrazolo(1,5-A)
pyrimidine, 3-(phenyl)-6-(4-pyridyl) pyrazolo(1,
5-A)**pyrimidine**, or 3-(phenyl)-6-(2-(3-carboxy)pyridyl)
pyrazolo(1,5-A)**pyrimidine**; or a
pharmaceutically acceptable salt thereof.
13. A method according to claim 12 wherein the inflammatory disease is
selected from **rheumatoid arthritis**, psoriasis,
contact dermatitis and delayed hypersensitivity reactions.

L10 ANSWER 8 OF 25 IFIPAT COPYRIGHT 2003 IFI
PI US 4912104 19900327 (CITED IN 001 LATER PATENTS)
ACLM 16. A compound according to claim 1, which is 6,8-diallyl-1-propionyl-2,3-
dihydro-1H-imidazo(2',1':5,1)pyrazolo(3,4-
pyrimidine-7,9(6H,8H)-dione.
21. A method for treatment or amelioration of chronic **rheumatoid
arthritis**, lumbago, or neck-shoulder-arm syndrome in a mammal,
which comprises administering to said mammal an effective amount of a
compound as. . .

L10 ANSWER 9 OF 25 SCISEARCH COPYRIGHT 2003 THOMSON ISI
SO PHOSPHORUS SULFUR AND SILICON AND THE RELATED ELEMENTS, (**1996**)
Vol. 110, No. 1-4, pp. 229-232.
ISSN: 0308-664X.
AB In the course of research toward a safe and effective treatment for
rheumatoid arthritis, we identified new pyrazolo[
1,5-a]**pyrimidine** and 4-pyrimidinone
bisphosphonate esters, which are potent inhibitors of a murine model of
chronic, cutaneous inflammation (delayed type hypersensitivity granuloma).
. .

L10 ANSWER 10 OF 25 TOXCENTER COPYRIGHT 2003 ACS
TI Preparation of pyrazolo[1,5-a]**pyrimidine**
derivatives as nitrogen monoxide synthase inhibitors
PI WO 9959998 A1 **25 Nov 1999**
SO (**1999**) PCT Int. Appl., 109 pp.
CODEN: PIXXD2.
AB Pyrazolo[1,5-a]**pyrimidine** derivs.
represented by general formula [I; R1 = lower alkyl, Ph, thienyl; one of
R2 and R3 = H and. . . nitrogen monoxide synthase inhibitory effect and
are useful as analgesic agents and remedies and preventives for sepsis,
endotoxin shock, chronic **rheumatoid arthritis**, etc.,
are prepd. Thus, 1.0 g di-Et (5-n-butylpyrazolo[1,5-a]pyrimidin-7-
yl)methylphosphonate and 0.66 g 3,4,5-trimethoxybenzaldehyde were
dissolved in 5.0 mL ethanol, cooled to. . .

RN . . . 78-38-6 (Diethyl ethylphosphonate)
86-81-7 (3,4,5-Trimethoxybenzaldehyde)
104-88-1 (4-Chlorobenzaldehyde)
106-48-9 (4-Chlorophenol)
108-98-5 (Thiophenol)
867-13-0 (Triethyl phosphonoacetate)
28460-01-7 (Diethyl methylthiomethylphosphonate)
57230-04-3 (3-Benzyloxy-4,5-dimethoxybenzaldehyde)
167371-63-3 (5-Butyl-7-chloropyrazolo[**1,5**-a]**pyrimidine**)
RN 251363-62-9; 251363-63-0; 251363-64-1; 251363-65-2; 251363-66-3; 251363-67-4; 251363-68-5; 251363-69-6; 251363-70-9; 251363-71-0; 251363-72-1; 251363-73-2; 251363-74-3; 251363-75-4; 251363-76-5; 251363-77-6; 251363-78-7; 251363-79-8; 251363-80-1; 251363-81-2;. . .

L10 ANSWER 11 OF 25 USPATFULL
PI US 6518267 B1 20030211
WO 9959526 19991125 <--
AB . . . bone loss or cartilage or matrix degradation, including osteoporosis; gingival disease including gingivitis and periodontitis; arthritis, more specifically, osteoarthritis and **rheumatoid arthritis**; Paget's disease; hypercalcemia of malignancy; and metabolic bone disease, comprising inhibiting said bone loss or excessive cartilage or matrix degradation. . .
SUMM . . . may also be useful for treating diseases of excessive cartilage or matrix degradation, including, but not limited to, osteoarthritis and **rheumatoid arthritis**. Metastatic neoplastic cells also typically express high levels of proteolytic enzymes that degrade the surrounding matrix. Thus, selective inhibition of. . .
SUMM . . . osteoporosis and gingival diseases, such as gingivitis and periodontitis, or by excessive cartilage or matrix degradation, such as osteoarthritis and **rheumatoid arthritis**.
SUMM 2,7-dimethylpyrazolo[**1,5**-a]**pyrimidine** and
SUMM 1N-(N-(2,7-dimethylpyrazolo[**1,5**-a]**pyrimidine**-6-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one;
SUMM 1N-(N-(pyrimidine-4-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(2,7-dimethylpyrazolo[**1,5**-a]**pyrimidine**-6-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one;
SUMM . . . diseases of excessive bone or cartilage loss, including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and **rheumatoid arthritis**, Paget's disease; hypercalcemia of malignancy, and metabolic bone disease.
SUMM . . . diseases of excessive bone or cartilage loss, including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and **rheumatoid arthritis**. Paget's disease, hypercalcemia of malignancy, and metabolic bone disease.
DETD Preparation of 1N-(N-(2,7-Dimethylpyrazolo[**1,5**-a]**pyrimidine**-6-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one
DETD a) 1N-(N-(2,7-Dimethylpyrazolo[**1,5**-a]**pyrimidine**-6-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one
DETD Following the procedure of Example 4(a-d), except substituting "2,7-dimethylpyrazolo[**1,5**-a]**pyrimidine**-6-carboxylic acid" for "thianaphthenyl-2-carboxylic acid", gave the title compound: MS (ES+) 570.2 (M+H.sup.+).
CLM What is claimed is:
. . . phenyl, thiophene, benzthiazole, 2, 3, 4, 5, 6, or 7 quinoline,

naphthyl, C.sub.0-C.sub.6alkyl pyrazole, N-methyl pyrrole, and benzoxazole; pyrazine; pyrimidine; 2,7-dimethylpyrazolo[1,5-a]**pyrimidine** and 4,7-dimethylpyrazolo[5,1-c][1,2,4]-triazine, R.sub.6 is selected from the group consisting of: phenyl and phenyl substituted with C.sub.0-C.sub.6 alkyl, N-piperidine, benzofuran; or. . .

. . . (S)-3N-(N-(5-Methoxycarbonylbenzofuryl-2-carbonyl)-L-leucinyl)amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-butanone; (S)-3N-[N-{4-Methoxy-3-(N,N-dimethylaminoethyl)oxy}benzoyl-L-leucinyl]amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-butanone; (S)-3N-[N-(3-(4-Methylpiperazinyl))-benzoyl}-L-leucinyl]amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-propanone; (S)-3N-[N-{(N-Methyl-N'-(4-(1-methylpiperidinyl)amino}benzoyl}-L-leucinyl]amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-butanone; (S)-3N-[N-{(N-Methyl-N'-(beta-N,N-dimethylaminoethyl)amino}benzoyl-L-leucinyl]amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-butanone; (S)-3N-[N-(5-(Morpholinoethyloxy)benzofuryl-2-carbonyl)-L-leucinyl]amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-butanone; (S)-3N-{N-(4-Methyl[4-trifluoromethyl)phenyl]thiazole-5-carbonyl)-L-leucinyl)]}-amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-butanone; 1N-(N-(biphenyl)-4-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(indole-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(indole-6-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(adamantane-1-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl-amino-propan-2-one; 1N-(N-(1-methoxy-2-naphthoyl)-leucine)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(thieno[3,2-b]thiophene-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4-cyclohexylbenzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(1-methylpyrrole-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenyacetyl)-amino-propan-2-one; 1N-(N-(4-methoxybenzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(thiophene-3-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4-(4'-ethylbiphenyl)carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(pyrazine-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(2,7-dimethylpyrazolo[1,5-a]**pyrimidine**-6-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4,7-dimethylpyrazolo[5,1-c][1,2,4]triazine-3-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-thianaphthenyl-2-carbonyl)-leucinyl)-amino-3N-(3-(6-methyl-2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-thianaphthenyl-2-carbonyl)-leucinyl)-amino-3N-(3-(5-methyl-2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4-trifluoromethylbenzoyl)-leucinyl)-amino-3N-(3-(6-methyl-2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4-trifluoromethylbenzoyl)-leucinyl)-amino-3N-(3-(4-methyl-2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(N-tert-butoxycarbonyl-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-((2-dimethylamino)ethoxy)-benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-((2-dimethylamino)ethoxy)-3-methoxy-benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-(dimethylaminoethoxy)benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-((2-dimethylamino)ethoxy)-4-methoxy-benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-((2-(piperidinyl)ethoxy)4-methoxy-benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(1,2,3,4-tetrahydroisoquinoline-2-carbonyl)-leucinyl)-amino-3N-(3-(2-

pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(piperazine-1-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-methylpiperazine-1-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-phenoxybenzenesulfonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-methoxy-3-(2-(4-morpholinyl)ethoxy)benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-methoxy-2-naphthoyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(cyclohexene-1-carbonyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-(benzoyl)benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-(phenylmethoxy)benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one;. . .

. . . (S)-3N-[N-{4-Methoxy-3-(N,N-dimethylaminoethyl)oxy}benzoyl-L-leucinyl]amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-butanone; (S)-3N-[N-(3-(4-Methylpiperazinyl))-benzoyl}-L-leucinyl]amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-propanone; (S)-3N-[N-{(N-Methyl-N'-(4-(1-methylpiperidinyl)amino)benzoyl}-L-leucinyl]amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-butanone; (S)-3N-[N-{(N-Methyl-N'-(beta-N,N-dimethylaminoethyl)amino}benzoyl-L-leucinyl]amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-butanone; (S)-3N-[N-(5-(Morpholinoethyloxy)benzofuryl-2-carbonyl)-L-leucinyl]amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-butanone; (S)-3N-{N-(4-Methyl[4-trifluoromethyl)phenyl]thiazole-5-carbonyl)-L-leucinyl)]}-amino-1N-[3-(2-pyridyl)phenylacetyl]amino-2-butanone; 1N-(N-(biphenyl)-4-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(indole-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(indole-6-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(adamantane-1-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(1-methoxy-2-naphthoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(thieno[3,2-b]thiophene-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4-cyclohexylbenzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(1-methylpyrrole-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4-methoxybenzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(thiophene-3-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4-(4'-ethylbiphenyl)carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(pyrazine-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(pyrimidine-4-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(2,7-dimethylpyrazolo[1,5-a]**pyrimidine**-6-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4,7-dimethylpyrazolo[5,1-c][1,2,4]triazine-3-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-thianaphthenyl-2-carbonyl)-leucinyl)-amino-3N-(3-(6-methyl-2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-thianaphthenyl-2-carbonyl)-leucinyl)-amino-3N-(3-(5-methyl-2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4-trifluoromethylbenzoyl)-leucinyl)-amino-3N-(3-(6-methyl-2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-(4-trifluoromethylbenzoyl)-leucinyl)-amino-3N-(3-(4-methyl-2-pyridyl)-phenylacetyl)-amino-propan-2-one; 1N-(N-tert-butoxycarbonyl-leucinyl)-amino-3N-(4-nitrophenylmethoxycarbonyl)-amino-propan-2-one; 1N-(N-(4-((2-dimethylamino)ethoxy)-benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-((2-dimethylamino)ethoxy)-3-methoxy-benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-(dimethylaminoethoxy)benzoyl)-leucinyl)-amino-3N-(3-(2-

pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-((2-dimethylamino)ethoxy)4-methoxy-benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-((2-(piperidinyl)ethoxy)-4-methoxy-benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-phenylpropionyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(1,2,3,4-tetrahydroisoquinoline-2-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(piperazine-1-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-methylpiperazine-1-carbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-((2-pyridyl)methoxycarbonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-phenoxybenzenesulfonyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(4-methoxy-3-(2-(4-morpholinyl)ethoxy)benzoyl)-leucinyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(3-methoxy-2-naphthoyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one; 1N-(N-(cyclohexene-1-carbonyl)-amino-3N-(3-(2-pyridyl)phenylacetyl)-amino-propan-2-one;. . .

18. A method according to claim 16 wherein said disease is **rheumatoid arthritis**.

25. A method according to claim 23 wherein said disease is **rheumatoid arthritis**.

L10 ANSWER 12 OF 25 USPATFULL

PI US 6509361 B1 20030121
WO 9958523 19991118 <--

SUMM . . . implicated in mediating a number of diseases. Recent studies indicate that TNF has a causative role in the pathogenesis of **rheumatoid arthritis**. Additional studies demonstrate that inhibition of TNF has broad application in the treatment of inflammation, inflammatory bowel disease, multiple sclerosis. . .

SUMM . . . monocytes and macrophages and is also involved in the inflammatory response. IL-1 plays a role in many pathophysiological responses including **rheumatoid arthritis**, fever and reduction of bone resorption.

SUMM . . . Jan. 12, 1995, describes novel pyrazole compounds having agrohorticultural bactericidal effect. U.S. Pat. No. 5,201,938, to Costales, describes novel substituted N-pyrazolyl-1,2,4-triazolo[**1,5**-c]-**pyrimidine**-2-sulfonamide compounds and their use as herbicides. WO 93/09100, published May 13, 1993, describes trizolocarboxamides with herbicidal activity used to control. . .

SUMM Excessive or unregulated TNF production has been implicated in mediating a number of diseases, including **rheumatoid arthritis**, inflammation, inflammatory bowel disease, multiple sclerosis, asthma, and viral infections. IL-8 is another pro-inflammatory cytokine, and is associated with conditions including inflammation. Additionally, IL-1 is involved in the inflammatory response. IL-1 plays a role in many pathophysiological responses including **rheumatoid arthritis**, fever and reduction of bone resorption. TNF-, IL-1 and IL-8 affect a wide variety of cells and tissues and are. . .

SUMM . . . antipyretic for the treatment of fever. Compounds of the invention is useful to treat arthritis, including but not limited to, **rheumatoid arthritis**, spondyloarthropathies, gouty arthritis, osteoarthritis, systemic lupus erythematosus and juvenile arthritis, osteoarthritis, gouty arthritis and other arthritic conditions. Such compounds are. . .

L10 ANSWER 13 OF 25 USPATFULL

PI US 6380203 B1 20020430
WO 9854093 19981203 <--

SUMM . . . to hyperproliferative disorders which are initiated/maintained by aberrant tyrosine kinase enzyme activity. Examples include psoriasis, cancer, immunoregulation (graft rejection), atherosclerosis, **rheumatoid arthritis**, angiogenesis (e.g. tumor growth, diabetic retinopathy), etc.

SUMM 3-(4-fluorophenyl)-6-(4-pyridyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(3-chlorophenyl)-6-(4-pyridyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(3,4-methylenedioxypheny)-6-(4-pyridyl) pyrazolo(**1,5** -A)**pyrimidine**,

SUMM 3-(phenyl)-6-(4-pyrimidyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(4-fluorophenyl)-6-(4-pyrimidyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(3-chlorophenyl)-6-(4-pyrimidyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(3-thienyl)-6-(4-pyrimidyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(3-acetamidophenyl)-6-(4-methylphenyl) pyrazolo(**1,5** -A)**pyrimidine**,

SUMM 3-(phenyl)-6-(4-methoxyphenyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(3-acetamidophenyl)-6-(4-methoxyphenyl)pyrazolo(**1,5** -A)**pyrimidine**,

SUMM 3-(3-thienyl)-6-(4-methoxyphenyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(phenyl)-6-(4-methoxyphenyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(4-pyridyl)-6-(4-methoxyphenyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(phenyl)-6-(4-chmorophenyl) pyrazolo(**1,5**-A) **pyrimidine**.

SUMM 3-(4-pyridyl)-6-(4-chlorophenyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(phenyl)-6-(4-methylphenyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(4-pyridyl)-6-(4-methylphenyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(4phenyl)-6-(2-pyridyl) pyrazolo(**1,5**- A) **pyrimidine**,

SUMM 3-(4-pyridyl)-6-(2-pyridyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(phenyl)-6-(4-pyrimidyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(4-pyridyl)-6-(4-pyrimidyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(phenyl)-6-(2-pyrazinyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(4-pyridyl)-6-(2-pyrazinyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(3-pyridyl)-6-(4-methoxyphenyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(phenyl)-6-(4-pyridyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(3-pyridyl)-6-(4-pyridyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(4 pyridyl)-6-(4-methoxyphenyl) pyrazolo(**1,5**-A) **pyrimidine**,

SUMM 3-(3-thienyl)-6-(4-methoxyphenyl) pyrazolo(**1,5**-A)

pyrimidine,
SUMM 3-(3-thienyl)-6-(4-hydroxyphenyl)pyrazolo(**1,5**-A)
pyrimidine,
SUMM 3-(3-thienyl)-6-(4-(2-(4-morpholinyl)ethoxy)phenyl) pyrazolo(**1**
,5-A)**pyrimidine**,
SUMM 3-(3-thienyl)-6-(cyclohexyl)pyrazolo (**1,5**-A)
pyrimidine,
SUMM 3-(bromo)-6-(4-methoxyphenyl) pyrazolo(**1,5**-A)
pyrimidine,
SUMM 3-(bromo)-6-(4-pyrimidyl) pyrazolo(**1,5**-A)
pyrimidine,
SUMM 3-(phenyl)-6-(2-(3-carboxy)pyridyl) pyrazolo(**1,5**-A)
pyrimidine, and
SUMM 3-(3-thienyl)-6-(4-pyridyl) pyrazolo(**1,5**-A)
pyrimidine.
SUMM . . . to form powders. Such topical formulations can be used to treat ocular diseases as well as inflammatory diseases such as **rheumatoid arthritis**, psoriasis, contact dermatitis, delayed hypersensitivity reactions and the like.
DETD ##STR8## 3-(4 pyridyl)-6-(4-methoxyphenyl) pyrazolo(**1,**
5-A)**pyrimidine**
DETD 3-(3-thienyl)-6-(4-methoxyphenyl) pyrazolo(**1,5**-A)
pyrimidine
DETD 3-(3-thienyl)-6-(4-hydroxyphenyl)pyrazolo(**1,5**-A)
pyrimidine Ethanethiol (30 mg, 36 uL) was added dropwise over 1 min to a suspension of sodium hydride (23 mg, 0.98. . .
DETD 3-(3-thienyl)-6-(4-(2-(4-morpholinyl)ethoxy)phenyl) pyrazolo(**1**
,5-A)**pyrimidine**
DETD 3-(3-thiophenyl)-7-(4-pyridyl) pyrazolo(**1,5**-A)
pyrimidine
DETD 3-(3-thienyl)-6-(cyclohexyl) pyrazolo(**1,5**-A)
pyrimidine
CLM What is claimed is:
2. A compound in accordance with claim 1 which is: 3-(4-fluorophenyl)-6-(4-pyridyl) pyrazolo(**1,5**-A)**pyrimidine**,
3-(3-chlorophenyl)-6-(4-pyridyl) pyrazolo(**1,5**-A)
pyrimidine, 3-(3,4-methylenedioxyphenyl)-6-(4-pyridyl) pyrazolo(
1,5-A)**pyrimidine**, 3-(phenyl)-6-(4-pyrimidyl)
pyrazolo(**1,5**-A)**pyrimidine**,
3-(4-fluorophenyl)-6-(4-pyrimidyl) pyrazolo(**1,5**-A)
pyrimidine, 3-(3-chlorophenyl)-6-(4-pyrimidyl) pyrazolo(
1,5-A)**pyrimidine**, 3-(3-acetamidophenyl)-6-(4-
methylphenyl) pyrazolo(**1,5**-A)**pyrimidine**,
3-(phenyl)-6-(4-methoxyphenyl) pyrazolo(**1,5**-A)
pyrimidine, 3-(3-acetamidophenyl)-6-(4-methoxyphenyl)pyrazolo(
1,5-A)**pyrimidine**, 3-(phenyl)-6-(4-
methoxyphenyl) pyrazolo(**1,5**-A)**pyrimidine**,
3-(phenyl)-6-(4-chlorophenyl) pyrazolo(**1,5**-A)
pyrimidine, 3-(phenyl)-6-(4-methylphenyl) pyrazolo(**1,**
5-A)**pyrimidine**, 3-(phenyl)-6-(2-pyridyl) pyrazolo(
1,5-A)**pyrimidine**, 3-(phenyl)-6-(4-pyrimidyl)
pyrazolo(**1,5**-A)**pyrimidine**,
3-(phenyl)-6-(2-pyrazinyl) pyrazolo(**1,5**-A)
pyrimidine, 3-(phenyl)-6-(4-pyridyl) pyrazolo(**1,**
5-A)**pyrimidine**, or 3-(phenyl)-6-(2-(3-carboxy)pyridyl)
pyrazolo(**1,5**-A)**pyrimidine**; or a
pharmaceutically acceptable salt thereof.

13. A method according to claim 12 wherein the inflammatory disease is selected from **rheumatoid arthritis**, psoriasis,
contact dermatitis and delayed hypersensitivity reactions.

L10 ANSWER 14 OF 25 USPATFULL
PI US 6015578 20000118
WO 9632111 19961017 <--
SUMM . . . diseases which may be influenced favourably by the action of an immunomodulatory active ingredient. Chemically, the substance Trapidil is an N,N-diethyl-5-methyl-s-triazolo[**1**,**5**-a]-**pyrimidine**. Its clinical-pharmacological activity as known so far extends to the treatment of coronary cardiac diseases both in case of acute. . .
SUMM In view of its triazolo[**1**,**5**-a)-**pyrimidine** structure, Trapidil holds a special position among coronary therapeutic agents, because it is the only active ingredient with this particular. . .
DETD . . . Trapidil are lymphatic oedemas, myx oedemas, sclerodermia, calcinosis cutis, Kawasaki disease, disorders caused by the deposition of immunocomplexes such as **rheumatoid arthritis**, systemic lupus erythematodes, periarteritis nodosa, poly- and dermatomyositis, diffuse fibrotic alveolitis, certain forms of glomerulopathy, lepra, trypanosomiasis, chronic-aggressive hepatitis and. . .

L10 ANSWER 15 OF 25 USPATFULL
PI US 5643895 19970701 <--
SUMM . . . by abnormal phosphate and calcium metabolism, and as a treatment of inflammation. These diseases include osteoporosis, Paget's disease, periodontal disease, **rheumatoid arthritis**, osteoarthritis, neuritis, bursitis, soft tissue mineral disorders, ankylosing spondylitis, atherosclerosis, multiple myeloma of bone, metastatic bone disease, and mitral valve. . .
SUMM . . . in humans and lower animals as a safe and effective treatment of chronic inflammatory diseases. These diseases include periodontal disease, **rheumatoid arthritis**, osteoarthritis, pneumoconioses, Crohn's disease, chronic inflammatory bowel disease, chronic asthma, atherosclerosis, multiple sclerosis, and sarcoidosis.
DETD Pyrazolo(**1**,**5**-a)**pyrimidine**-7-butanoic acid, 3-cyano-.alpha.-(dimethoxyphosphinyl)-2,5-dimethyl-, methyl ester
DETD The reaction of trimethylphosphonoacrylate and a pyrazolopyrimidine was carried out as follows. 2,5,7-Trimethylpyrazolo(**1**,**5**-a)**pyrimidine**-3-carbononitrile (0.96 g, 5.15 mmol) was stirred in pyridine (10 ml) under nitrogen and cooled in an ice-ethanol bath. A solution. . . SO.sub.4), filtered and evaporated to give a gum (1.57 g) which crystallized upon addition of methyl-t-butyl ether. The resultant solid Pyrazolo(**1**,**5**-a)**pyrimidine**-7-butanoic acid, 3-cyano-.alpha.-(dimethoxyphosphinyl)-2,5-dimethyl-, methyl ester (1.21 g, 62%) was recrystallized from acetone-hexane as cream crystals mp 164.degree.-5.degree..

L10 ANSWER 16 OF 25 USPATFULL
PI US 5635495 19970603 <--
WO 9409017 19940428 <--
SUMM . . . by abnormal phosphate and calcium metabolism, and as a treatment of inflammation. These diseases include osteoporosis, Paget's disease, periodontal disease, **rheumatoid arthritis**, osteoarthritis, neuritis, bursitis, soft tissue mineralization disorders, ankylosing spondylitis, atherosclerosis, multiple myeloma of bone, metastic bone disease, and mitral valve. . .
SUMM . . . its associated symptoms such as inflammation and excessive bone growth or remodeling. These diseases include osteoporosis, Paget's disease, periodontal disease, **rheumatoid arthritis**, osteoarthritis, neuritis, bursitis, soft tissue mineralization disorders, ankylosing spondylitis, atherosclerosis, multiple myeloma of

bone, metastic bone disease, and mitral valve. . .

DETD Pyrazolo(1,5-a)**pyrimidine** is suspended in pyridine at 0.degree. C. and treated with a solution of LiHMDS. After stirring at 0.degree. C. for. . .

DETD 5,7-dimethyl-2-phenyl-pyrazolo(1,5-a) **pyrimidine**-3-carbonitrile in pyridine at 0.degree. C. is treated with LiHMDS and stirred for 30 minutes. The deep red solution is treated. . .

DETD 3-Bromo-2,5,7-trimethyl-pyrazolo(1,5-a) **pyrimidine** is dissolved in THF at 0.degree. C. and treated with LiHMDS. After stirring for 30 minutes, EMP phosphonic acid in. . .

DETD 2,5,7-Trimethyl-3-nitro-pyrazolo(1,5-a) **pyrimidine** is dissolved in pyridine at 0.degree. C., then treated with LiHMDS. After stirring for 30 minutes, EMP phosphonic acid in. . .

DETD Pyrazolo (1,5-a)**pyrimidine** in pyridine at 0.degree. C. is treated with LiHMDS and stirred for 30 minutes. EMP phosphonic acid is added, the. . .

L10 ANSWER 17 OF 25 USPATFULL

PI US 5624931 19970429 <--

SUMM . . . can be used for prophylactic and therapeutic treatment of IL-1 and TNF mediated diseases such as chronic inflammatory diseases (e.g. **rheumatoid arthritis**, osteoarthritis, etc.) osteoporosis, rejection by transplantation, asthma, endotoxin shock, specific autoimmune diseases [e.g. ankylosing spondylitis, autoimmune hematological disorders (e.g. hemolyticodo. . .

DETD . . . dried and concentrated in vacuo. The residue was crystallized from a mixture of ethyl acetate and diethyl ether to yield 2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[1,5-a] **pyrimidine** (102 mg).

DETD (2) 2-(4-Fluorophenyl)-3-(pyrimidin-4-yl)pyrazolo[1,5 -a]**pyrimidine**

DETD (1) A mixture of 2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[1 ,5-a]**pyrimidine** (56 mg) and sodium borohydride (16 mg) in ethanol (2 ml) was refluxed for 2 hours, cooled, and poured into. . . dried and concentrated in vacuo. The residue was crystallized from a mixture of ethyl acetate and ethyl ether to yield 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a] **pyrimidine** (44 mg).

DETD (2) 2-(4-Fluorophenyl)-3-(pyrimidin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine**

DETD To a suspension of 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (100 mg) in methanol (2 ml) was added 10% methanolic hydrogen chloride (0.5 ml). The resulting clear solution was concentrated. . . the solution was concentrated in vacuo. The residue was crystallized from a mixture of ethanol and diethyl ether to give 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** dihydrochloride (100 mg).

DETD (1) 2-(4-Methylthiophenyl)-3-(pyridin-4-yl)pyrazolo-[1, 5-a]**pyrimidine**

DETD (2) 2-(4-Fluorophenyl)-3-(2-fluoropyridin-4-yl)pyrazolo[1, 5-a]**pyrimidine**

DETD (3) 2-(4-Fluorophenyl)-3-(3-methylpyridin-4-yl)pyrazolo-[1, 5-a]**pyrimidine**

DETD (4) 3-(4-Fluorophenyl)-2-(pyridin-4-yl)pyrazol[1,5 -a]**pyrimidine**

DETD (5) 2-(4-Fluorophenyl)-3-(pyridin-2-yl)pyrazolo[1,5 -a]**pyrimidine**

DETD (6) 2-(4-Fluorophenyl)-3-(pyridin-3-yl)pyrazolo[1,5 -a]**pyrimidine**

DETD (1) 3-(4-Fluorophenyl)-2-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine**

DETD (2) 2-(4-Methylthiophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine**

DETD (3) 2-(4-Fluorophenyl)-3-(2-fluoropyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine**

DETD (4) 2-(4-Fluorophenyl)-3-(3-methylpyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine**

DETD (5) 2-(4-Fluorophenyl)-3-(2-methylpyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine**

DETD (6) 2-(4-Fluorophenyl)-3-(pyridin-2-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine**

DETD (7) 2-(4-Fluorophenyl)-3-(pyridin-3-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine**

DETD 2-(4-Fluorophenyl)-4-methyl-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine**

DETD . . . aqueous solution was neutralized with diluted hydrochloric acid. The separated solid was collected, washed with water and dried to give 4,5-dihydro-3-(4-fluorophenyl)-5-oxo-2-(pyridin-4-yl)pyrazolo[1,5-a]**pyrimidine** (62 mg).

DETD . . . neutralized with an aqueous saturated sodium bicarbonate solution. The separated solid was collected, washed with water and dried to give 2-(4-fluorophenyl)-5-oxo-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (750 mg).

DETD . . . of sodium hydride (60% dispersion in mineral oil, 35 mg) in dry N,N-dimethylformamide (5 ml) was added a solution of 2-(4-fluorophenyl)-5-oxo-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (250 mg) in dry N,N-dimethylformamide (3 ml) dropwise under ice cooling. The mixture was stirred for 30 minutes and to. . . on silica gel and the obtained crude solid was recrystallized from a mixture of dichloromethane and diisopropyl ether to give 2-(4-fluorophenyl)-4-methyl-5-oxo-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (180 mg).

DETD To a solution of 2-(4-methylthiophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (190 mg) in dichloromethane (6 ml) was added m-chloroperbenzoic acid (127 mg) under ice cooling. The mixture was stirred at. . . chromatography on silica gel and the obtained crude solid was recrystallized from a mixture of 2-propanol and ether to give 2-(4-methylsulfinylphenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (168 mg).

DETD To a solution of 2-(4-methylthiophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (190 mg) in dichloromethane (6 ml) was added m-chloroperbenzoic acid (318 mg) under ice cooling. The mixture was stirred at. . . chromatography on silica gel and the obtained crude solid was recrystallized from a mixture of 2-propanol and ether to give 2-(4-methylsulfonylphenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (63 mg).

DETD To a solution of 2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[1,5-a]**pyrimidine** (480 mg) in dry tetrahydrofuran (15 ml) was added acetyl chloride (0.89 ml) dropwise under ice cooling. The mixture was. . . washed with brine, dried and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give 3-(1-acetyl-1,2-dihydro-2-methylpyridin-4-yl)-2-(4-fluorophenyl)pyrazolo[1,5-a]**pyrimidine** (327 mg).

DETD A mixture of 3-(1-acetyl-1,2-dihydro-2-methylpyridin-4-yl)-2-(4-fluorophenyl)pyrazolo[1,5-a]**pyrimidine** (315 mg) and sulfur (146 mg) in decaline (3 ml) was stirred at

190.degree. C. for 2 hours. The reaction mixture was cooled and purified by column chromatography on silica gel to give 2-(4-fluorophenyl)-3-(2-methylpyridin-4-yl)pyrazolo[1,5-a]**pyrimidine** (135 mg) as crystals.

DETD A mixture of 3-(4-fluorophenyl)-2-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (100 mg), triethylamine (0.4 ml) and acetic anhydride (0.2 ml) in dry 1,2-dichloroethane (3 ml) was refluxed for 2 days.. . . residue was purified by column chromatography on silica gel and the obtained oil was crystallized from diisopropyl ether to give 4-acetyl-3-(4-fluorophenyl)-2-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (60 mg).

DETD 2-(4-Fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** dihydrochloride (183 mg) was dissolved in hot aqueous isopropyl alcohol solution 15.5 ml). The solution was cooled and the separated solid was collected, washed with isopropyl alcohol and dried to give 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** hydrochloride 182 mg).

DETD To a suspension of 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (250 mg) in ethanol (3.5 ml) was added 1N hydrochloric acid (0.85 ml). The resulting clear solution was concentrated in. . . mixture of methanol (0.5 ml) and ethyl acetate (3 ml) and recrystallized from an aqueous isopropyl alcohol solution to give 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** hydrochloride (233 mg).

DETD . . . The residue was purified by column chromatography on silica gel and the obtained oil was crystallized from methanol to give 5,7-diphenyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[1,5-a]**pyrimidine** (250 mg).

DETD . . . chromatography on silica gel and the obtained oil was crystallized from a mixture of ethyl acetate and hexane to give 6,7-dihydro-2-(4-fluorophenyl)-3-(pyridin-4-yl)-5,7,7-trimethylpyrazolo[1,5-a]**pyrimidine** (83 mg).

DETD . . . 1N-hydrochloric acid (4 ml) and water (6 ml). The separated solid was collected, washed with water and dried to give 5,7-dihydroxy-2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[1,5-a]**pyrimidine** (210 mg).

DETD . . . the reaction mixture was diluted with ethanol to crystallize. The crude crystalline was collected and washed with ethanol to give 4,7-dihydro-2-(4-fluorophenyl)-5-methyl-7-oxo-3-(pyridin-4-yl)pyrazolo[1,5-a]**pyrimidine** (104 mg).

DETD . . . refluxed for 1 hour. The reaction mixture was concentrated in vacuo and the residue was crystallized from ethanol to give 7-amino-6-cyano-2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[1,5-a]**pyrimidine** (77 mg).

DETD . . . (10 ml) was refluxed for 3 hours. After cooling, the crude crystalline was obtained and washed with ethanol to give 4,7-dihydro-6-ethoxycarbonyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)-7-oxopyrazolo[1,5-a]**pyrimidine** (1.23 g).

DETD To a mixture of 4,7-dihydro-6-ethoxycarbonyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)-7-oxopyrazolo[1,5-a]**pyrimidine** (100 mg) in tetrahydrofuran (4 ml) was added lithium borohydride (2 mole in tetrahydrofuran, 0.26 ml) at room temperature and. . . acetate. The extracts were washed with brine, dried and concentrated in vacuo. The residue was crystallized from ethanol to give 6-ethoxycarbonyl-2-(4-fluorophenyl)-7-oxo-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (40 mg).

DETD A mixture of 4,7-dihydro-6-ethoxycarbonyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)-7-oxopyrazolo[1,5-a]**pyrimidine** (946

mg) in sulfuric acid (40% in water, 5 ml) was refluxed for 2 hours. After cooling, the pH of. . . 5 with an aqueous saturated sodium bicarbonate solution. The crude crystalline was obtained and washed with hot ethanol to give 4,7-dihydro-6-carboxy-2-(4-fluorophenyl)-3-(pyridin-4-yl)-7-oxopyrazolo[**1,5**-a]**pyrimidine** (275 mg).

DETD . . . 1N-hydrochloric acid (2 ml) and water (5 ml). The separated solid was collected, washed with water and dried to give 7-amino-2-(4-fluorophenyl)-5-hydroxy-3-(pyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine** (270 mg).

DETD 4-Acetyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

L10 ANSWER 18 OF 25 USPATFULL

PI US 5565441 19961015 <--

SUMM . . . by abnormal phosphate and calcium metabolism, and as a treatment of inflammation. These diseases include osteoporosis, Paget's disease, periodontal disease, **rheumatoid arthritis**, osteoarthritis, neuritis, bursitis, soft tissue mineral disorders, ankylosing spondylitis, atherosclerosis, multiple myeloma of bone, metastatic bone disease, and mitral valve. . .

SUMM . . . in humans and lower animals as a safe and effective treatment of chronic inflammatory diseases. These diseases include periodontal disease, **rheumatoid arthritis**, osteoarthritis, pneumoconioses, Crohn's disease, chronic inflammatory bowel disease, chronic asthma, atherosclerosis, multiple sclerosis, and sarcoidosis.

DETD Pyrazolo(**1,5**-a)**pyrimidine**-7-butanoic acid, 3-cyano-.alpha.-(dimethoxyphosphinyl)-2,5-dimethyl-, methyl ester

DETD The reaction of trimethylphosphonoacrylate and a pyrazolopyrimidine was carried out as follows. 2,5,7-Trimethylpyrazolo(**1,5**-a)**pyrimidine**-3-carbononitrile (0.96 g, 5.15 mmol) was stirred in pyridine (10 ml) under nitrogen and cooled in an ice-ethanol bath. A solution. . .

DETD . . . SO.sub.4), filtered and evaporated to give a gum (1.57 g) which crystallized upon addition of methyl-t-butyl ether. The resultant solid Pyrazolo(**1,5**-a)**pyrimidine**-7-butanoic acid, 3-cyano-.alpha.-(dimethoxyphosphinyl)-2,5-dimethyl-, methyl ester (1.21 g, 62%) was recrystallized from acetone-hexane as cream crystals mp 164.degree.-5.degree..

CLM What is claimed:

. . . a. 3-Pyridinepentanoic acid, .alpha.-(dimethoxyphosphinyl)-.delta.-oxo-, methyl ester; b. 2-Pyrimidinebutanoic acid, .alpha.-(dimethoxyphosphinyl)-1,6-dihydro-1-methyl-6-oxo-4-phenyl-, methyl ester; c. 2-Pyrimidinebutanoic acid, .alpha.-(dimethoxyphosphonic acid)-1,6-dihydro-1-methyl-6-oxo-4-phenyl-, methyl ester; d. Pyrazolo(**1,5**-a)**pyrimidine**-7-butanoic acid, 3-cyano-.alpha.-(dimethoxyphosphinyl)-2,5-dimethyl-, methyl ester; e. 2-Pyrimidinebutanoic acid, .alpha.-(dimethoxyphosphinyl)-1,6-dihydro-1-methyl-6-oxo-4-phenyl; f. 2-Pyrimidinebutanoic acid, 1,6-dihydro-1-methyl-6-oxo-4-phenyl-.alpha.-phosphono; g. 2-Pyrimidine butanoic acid, .alpha.-(dimethoxyphosphinyl)-1,6-dihydro-1-methyl-6-oxo-4-phenyl, dimethylethyl ester; and. . .

L10 ANSWER 19 OF 25 USPATFULL

PI US 5506233 19960409 <--
WO 9318042 19930916 <--

AB Macrolides of the FK-506 type and methods of treatment of resistance to transplantation, fungal infections, and autoimmune diseases such as **rheumatoid arthritis** and psoriasis using said macrolides.

SUMM . . . preventing or treating graft rejection following skin and organ transplant surgery and in preventing or treating autoimmune diseases

such as **rheumatoid arthritis** and psoriasis.
Additionally, these macrolide derivatives will find use in preventing or treating infectious diseases caused by fungi.

SUMM . . . preventing graft and transplant rejection. Further, this activity makes these compounds useful in preventing and treating autoimmune diseases such as **rheumatoid arthritis** and psoriasis in a mammal, especially man.

SUMM Additionally this invention embraces a method of treating autoimmune disease (such as **rheumatoid arthritis** or psoriasis) in a mammal in need of such treatment comprising administering to said mammal an effective amount of a. . .

SUMM Still further this invention embraces a pharmaceutical composition comprising an autoimmune disease (such as **rheumatoid arthritis** or psoriasis) treating effective amount of a compound of formula (I) and a pharmaceutically acceptable carrier.

SUMM . . . --OH is added rapidly. The reaction mixture is stirred for another 30 minutes to one hour and then 1.1 to **1.5** equivalents of 2-mercapto-**pyrimidine** is added. The reaction mixture is warmed to room temperature and stirred for about 16 to 24 hours. The product. . .

SUMM . . . compounds of formula (I) thus prepared are useful in the treatment of resistance to transplantation and autoimmune diseases such as **rheumatoid arthritis** or psoriasis. In the treatment of resistance to transplantation, a compound of formula (I) may be used either prophylactically or. . .

SUMM For use in the treatment of resistance to transplantation and autoimmune diseases such as **rheumatoid arthritis** or psoriasis in a mammal, including man, a compound of formula (I) is formulated into a suitable pharmaceutical composition containing. . .

SUMM . . . present invention as medical agents in the treatment of resistance to transplantation, fungal infectious diseases and autoimmune diseases such as **rheumatoid arthritis** or psoriasis is demonstrated by the activity of said compounds in the biological screens described hereinbelow. Said biological screen also. . . for determining dosage levels in mammals, including man, for the treatment of resistance to transplantation and autoimmune diseases such as **rheumatoid arthritis** and psoriasis,

SUMM . . . is indicative of usefulness of the active compound in the treatment of resistance to transplantation and autoimmune diseases such as **rheumatoid arthritis** and psoriasis.

L10 ANSWER 20 OF 25 USPATFULL

PI US 5478827 19951226 <--

SUMM . . . can be used for prophylactic and therapeutic treatment of IL-1 and TNF mediated diseases such as chronic inflammatory diseases (e.g. **rheumatoid arthritis**, osteoarthritis, etc.) osteoporosis, rejection by transplantation, asthma, endotoxin shock, specific autoimmune diseases [e.g. ankylosing spondylitis, autoimmune hematological disorders (e.g. hemolyticodo. . .

DETD . . . dried and concentrated in vacuo. The residue was crystallized from a mixture of ethyl acetate and diethyl ether to yield 2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[**1**,**5**-a] **pyrimidine** (102 mg).

DETD 2-(4-Fluorophenyl)-3-(pyrimidin-4-yl)pyrazolo[**1**,**5**-a] **pyrimidine**

DETD A mixture of 2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[**1**, **5**-a]**pyrimidine** (56 mg) and sodium borohydride (16 mg) in ethanol (2 ml) was refluxed for 2 hours, cooled, and poured into. . . dried and concentrated in vacuo. The residue was crystallized from a mixture of ethyl acetate and ethyl ether to yield 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1**,**5**-a] **pyrimidine** (44 mg).

DETD 2-(4-Fluorophenyl)-3-(pyrimidin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD To a suspension of 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** (100 mg) in methanol (2 ml) was added 10% methanolic hydrogen chloride (0.5 ml). The resulting clear solution was concentrated. . . the solution was concentrated in vacuo. The residue was crystallized from a mixture of ethanol and diethyl ether to give 2-(4-fluorophenyl)-3-(pyridin-4-yl)4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** dihydrochloride (100 mg).

DETD 2-(4-Methylthiophenyl)-3-(pyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine**

DETD 2-(4-Fluorophenyl)-3-(2-fluoropyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine**

DETD 2-(4-Fluorophenyl)-3-(3-methylpyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine**

DETD 3-(4-Fluorophenyl)-2-(pyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine**

DETD 2-(4-Fluorophenyl)-3-(pyridin-2-yl)pyrazolo[**1,5**-a]**pyrimidine**

DETD 2-(4-Fluorophenyl)-3-(pyridin-3-yl)pyrazolo[**1,5**-a]**pyrimidine**

DETD 3-(4-Fluorophenyl)-2-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD 2-(4-Methylthiophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD 2-(4-Fluorophenyl)-3-(2-fluoropyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD 2-(4-Fluorophenyl)-3-(3-methylpyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD 2-(4-Fluorophenyl)-3-(2-methylpyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD 2-(4-Fluorophenyl)-3-(pyridin-3-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD 2-(4-Fluorophenyl)-4-methyl-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD . . . aqueous solution was neutralized with diluted hydrochloric acid. The separated solid was collected, washed with water and dried to give 4,5-dihydro-3-(4-fluorophenyl)-5-oxo-2-(pyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine** (62 mg).

DETD . . . neutralized with an aqueous saturated sodium bicarbonate solution. The separated solid was collected, washed with water and dried to give 2-(4-fluorophenyl)-5-oxo-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** (750 mg).

DETD . . . of sodium hydride (60% dispersion in mineral oil, 35 mg) in dry N,N-dimethylformamide (5 ml) was added a solution of 2-(4-fluorophenyl)-5-oxo-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** (250 mg) in dry N,N-dimethylformamide (3 ml) dropwise under ice cooling. The mixture was stirred for 30 minutes and to. . . silica gel and the obtained crude solid was recrystallized from a mixture of dichloromethane and diisopropyl ether to give 2-(4-fluorophenyl)-4-methyl-5-oxo-3-(pyridin-4-yl)-4,5,6,7 -tetrahydropyrazolo[**1,5**-a]**pyrimidine** (180 mg).

DETD To a solution of 2-(4-methylthiophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** (190 mg) in dichloromethane (6 ml) was added m-chloroperbenzoic acid (127 mg) under ice cooling. The mixture was stirred at. . . chromatography on silica gel and the obtained crude solid was recrystallized from a mixture of 2-propanol and ether to give 2-(4-methylsulfinylphenyl)-3-

(pyridin-4-yl)4,5,6,7-tetrahydropyrazolo[**1,5**-a]
pyrimidine (168 mg).

DETD To a solution of 2-(4-methylthiophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** (190 mg) in dichloromethane (6 ml) was added m-chloroperbenzoic acid (318 mg) under ice cooling. The mixture was stirred at. . . chromatography on silica gel and the obtained crude solid was recrystallized from a mixture of 2-propanol and ether to give 2-(4-methylsulfonylphenyl)-3-(pyridin-4-yl)4,5,6,7-tetrahydropyrazolo[**1,5**-a]
pyrimidine (63 mg).

DETD To a solution of 2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine** (480 mg) in dry tetrahydrofuran (15 ml) was added acetyl chloride (0.89 ml) dropwise under ice cooling. The mixture was. . . washed with brine, dried and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give 3-(1-acetyl-1,2-dihydro-2-methylpyridin-4-yl)-2-(4-fluorophenyl)pyrazolo[**1,5**-a]**pyrimidine** (327 mg).

DETD A mixture of 3-(1-acetyl-1,2-dihydro-2-methylpyridin-4-yl)-2-(4-fluorophenyl)pyrazolo[**1,5**-a]**pyrimidine** (315 mg) and sulfur (146 mg) in decaline (3 ml) was stirred at 190.degree. C. for 2 hours. The reaction mixture was cooled and purified by column chromatography on silica gel to give 2-(4-fluorophenyl)-3-(2-methylpyridin-4-yl) pyrazolo[**1,5**-a]
pyrimidine (135 mg) as crystals.

DETD A mixture of 3-(4-fluorophenyl)-2-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** (100 mg), triethylamine (0.4 ml) and acetic anhydride (0.2 ml) in dry 1,2-dichloroethane (3 ml) was refluxed for 2 days.. . . residue was purified by column chromatography on silica gel and the obtained oil was crystallized from diisopropyl ether to give 4-acetyl-3-(4-fluorophenyl)-2-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]
pyrimidine (60 mg).

DETD 2-(4-Fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** dihydrochloride (183 mg) was dissolved in hot aqueous isopropyl alcohol solution (5.5 ml). The solution was cooled and the separated solid was collected, washed with isopropyl alcohol and dried to give 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** hydrochloride (82 mg).

DETD To a suspension of 2-(4-fluorophenyl)-3-(pyridin-4 -yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** (250 mg) in ethanol (3.5 ml) was added 1N hydrochloric acid (0.85 ml). The resulting clear solution was concentrated in. . . mixture of methanol (0.5 ml) and ethyl acetate (3 ml) and recrystallized from an aqueous isopropyl alcohol solution to give 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** hydrochloride (233 mg).

DETD . . . The residue was purified by column chromatography on silica gel and the obtained oil was crystallized from methanol to give 5,7-diphenyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine** (250 mg).

DETD . . . chromatography on silica gel and the obtained oil was crystallized from a mixture of ethyl acetate and hexane to give 6,7-dihydro-2-(4-fluorophenyl)-3-(pyridin-4-yl)-5,7,7-trimethylpyrazolo[**1,5**-a]**pyrimidine** (83 mg).

DETD . . . 1N-hydrochloric acid (4 ml) and water (6 ml). The separated solid was collected, washed with water and dried to give 5,7-dihydroxy-2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine** (210 mg).

DETD . . . the reaction mixture was diluted with ethanol to crystallize. The crude crystalline was collected and washed with ethanol to give

4,7-dihydro-2-(4-fluorophenyl)-5-methyl-7-oxo-3-(pyridin-4-yl)pyrazolo[1,5-a]**pyrimidine** (104 mg).

DETD . . . refluxed for 1 hour. The reaction mixture was concentrated in vacuo and the residue was crystallized from ethanol to give 7-amino-6-cyano-2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[1,5-a]**pyrimidine** (77 mg).

DETD . . . (10 ml) was refluxed for 3 hours. After cooling, the crude crystalline was obtained and washed with ethanol to give 4,7-dihydro-6-ethoxycarbonyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)-7-oxopyrazolo[1,5-a]**pyrimidine** (1.23 g).

DETD To a mixture of 4,7-dihydro-6-ethoxycarbonyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)-7-oxopyrazolo[1,5-a]**pyrimidine** (100 mg) in tetrahydrofuran (4 ml) was added lithium borohydride (2 mole in tetrahydrofuran, 0.26 ml) at room temperature and. . . acetate. The extracts were washed with brine, dried and concentrated in vacuo. The residue was crystallized from ethanol to give 6-ethoxycarbonyl-2-(4-fluorophenyl)-7-oxo-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine** (40 mg).

DETD A mixture of 4,7-dihydro-6-ethoxycarbonyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)-7-oxopyrazolo[1,5-a]**pyrimidine** (946 mg) in sulfuric acid (40% in water, 5 ml) was refluxed for 2 hours. After cooling, the pH of. . . 5 with an aqueous saturated sodium bicarbonate solution. The crude crystalline was obtained and washed with hot ethanol to give 4,7-dihydro-6-carboxy-2-(4-fluorophenyl)-3-(pyridin-4-yl)-7-oxopyrazolo[1,5-a]**pyrimidine** (275 mg).

DETD . . . 1N-hydrochloric acid (2 ml) and water (5 ml). The separated solid was collected, washed with water and dried to give 7-amino-2-(4-fluorophenyl)-5-hydroxy-3-(pyridin-4-yl)pyrazolo[1,5-a]**pyrimidine** (270 mg).

DETD 4-Acetyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]**pyrimidine**

L10 ANSWER 21 OF 25 USPATFULL

PI US 5397774 19950314 <--

SUMM . . . by abnormal phosphate and calcium metabolism, and as a treatment of inflammation. These diseases include osteoporosis, Paget's disease, periodontal disease, **rheumatoid arthritis**, osteoarthritis, neuritis, bursitis, soft tissue mineralization disorders, ankylosing spondylitis, atherosclerosis, multiple myeloma of bone, metastic bone disease, and mitral valve. . .

DETD Pyrazolo(1,5-a)**pyrimidine** (3.02 g, 16.2 mmol) was suspended in pyridine (40 ml) at 0.degree. C. and treated with a solution of LiHMDS. . .

DETD 5,7-dimethyl-2-phenyl-pyrazolo(1,5-a)**pyrimidine**-3-carbonitrile (621 mg, 2.50 mmol) in pyridine (5.0 mL) at 0.degree. C. was treated with LiHMDS (2.6 mL, 2.6 mmol) and. . .

DETD 3-Bromo-2,5,7-trimethyl-pyrazolo(1,5-a)**pyrimidine** (460 mg, 1.92 mmol) was dissolved in THF (10 mL) at 0.degree. C. and treated with LiHMDS (2.0 mL, 2.0. . .

DETD 2,5,7-Trimethyl-3-nitro-pyrazolo(1,5-a)**pyrimidine** (900 mg, 4.36 mmol) was dissolved in pyridine (10 mL) at 0.degree. C., then treated with LiHMDS (4.5 mL, 4.5. . .

DETD 5,7-Dimethyl-pyrazolo[1,5-a]**pyrimidine**-2-ol (3.26 g, 20 mmol) in pyridine (60 mL) at 0.degree. C. was treated with LiHMDS (42 mL, 42 mmol) and. . .

DETD B) The crude pyrazolo[1,5-a]**pyrimidine**-2-ol (475 mg, 1.02 mmol) in methylene chloride (5 mL) at 0.degree. C. was treated with benzoyl chloride (0.12 mL, 1.02. . .

DETD 5,7-Dimethyl-pyrazolo[1,5-a]**pyrimidine**

-2-ol (1.63 g, 10 mmol), potassium carbonate (690 mg, 5 mmol), and DMF (6 mL) were heated to 115.degree.-120.degree. C. for. . .

DETD 5,7-Dimethyl-pyrazolo[**1,5**-a]**pyrimidine**
-2-ol (1.63 g, 10 mmol), potassium carbonate (690 mg, 5 mmol), and DMF (6 mL) were heated to 115.degree.-120.degree. C. for. . .

DETD Pyrazolo (**1,5**-a)**pyrimidine** (1.25 g, 6.71
mmol) in pyridine (15 mL) at 0.degree. C. was treated with LiHMDS (8.1 mL, 8.1 mmol) and. . .

DETD Pyrazolo (**1,5**-a)**pyrimidine** (1.30 g, 6.98
mmol) in pyridine (15 mL) at 0.degree. C. was treated with LiHMDS (7.1 mL, 7.1 mmol) and. . .

L10 ANSWER 22 OF 25 USPATFULL

PI US 5366969 19941122 <--

SUMM . . . of heterotopic ossifications. Furthermore, due to their influencing of the calcium metabolism, they form a basis for the treatment of **rheumatoid arthritis**, of osteoarthritis and of degenerative arthrosis.

SUMM Especially preferred bicycles are the pyrido-(1,2-a)-pyrimidine-, oxazolo-(3,2-a)-pyrimidine-, thiazolo-(3,2-a)-pyrimidine-, 1,2,4-triazolo-(**1,5**-a)-**pyrimidine**-, pyrimido-(1,2-a)-pyrimidine-pyrimido-(2,1-b)-1,3-thiazine-and pyrimido-(1,2-a)-1,3-diazepine-diphosphonic acids.

SUMM 6,7-dihydro-1,2,4-triazolo-(1H)-(**1,5**-a)-**pyrimidine**-5,5-diphosphonic acid

DETD 6,7-Dihydro-(1H)-1,2,4-triazolo-(**1,5**-a)-**pyrimidine**-5,5-diphosphonic acid

CLM What is claimed is:

. . . of claim 4, wherein the bicyclic compound is selected from the group consisting of pyrido-(1,2-a)-pyrimidine-, diphosphonic acid, oxazolo-(3,2-a)-pyrimidine-, thiazolo-(3,2-a)-pyrimidine-diphosphonic acid, 1,2,4-triazolo-(**1,5**-a)-**pyrimidine**-diphosphonic acid, pyrimido-(1, 2-a)-pyrimidine-diphosphonic acid and pyrimido-(2,1-b)-1,3-thiazine-diphosphonic acid.

6. Compound of claim 1, wherein said compound is 3,4-dihydro-2H-pyrido-(1,2-a)-pyrimidine-2,2-diphosphonic acid; 3,4,6,7,8,9-hexahydro-2H-pyrido-(1,2-a)-pyrimidine-2,2-diphosphonic acid; 2,3,5,6-tetrahydro-7H-oxazolo-(3,2-a)-pyrimidine-7,7-diphosphonic acid; 6,7-dihydro-(1H)-1,2,4-triazolo-(**1,5**-a)-**pyrimidine**-5,5-diphosphonic acid; 3,4-dihydro-2H-pyrimido-(1,2-a)-pyrimidine-2,2-diphosphonic acid; 2-methyl-5,6-dihydro-1H-pyrimidine-4,4-diphosphonic acid; or 2-amino-1-methyl-5,6-dihydro-1H-pyrimidine-4,4-diphosphonic acid.

L10 ANSWER 23 OF 25 USPATFULL

PI US 5356897 19941018 <--

DETD . . . can be used for prophylactic and therapeutic treatment of IL-1 and TNF mediated diseases such as chronic inflammatory diseases (e.g. **rheumatoid arthritis**, osteoarthritis, etc.) osteoporosis, rejection by transplantation, asthma, endotoxin shock, specific autoimmune diseases [e.g. ankylosing spondylitis, autoimmune hematological disorders (e.g. hemolyticodo. . .

DETD . . . dried and concentrated in vacuo. The residue was crystallized from a mixture of ethyl acetate and diethyl ether to yield 2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine** (102 mg).

DETD (2) 2-(4-Fluorophenyl)-3-(pyrimidin-4-yl)pyrazolo[**1,5**-a]-**pyrimidine**

DETD (1) A mixture of 2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine** (56 mg) and sodium borohydride (16

mg) in ethanol (2 ml) was refluxed for 2 hours, cooled, and poured into. . . dried and concentrated in vacuo. The residue was crystallized from a mixture of ethyl acetate and ethyl ether to yield 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** (44 mg).

DETD (2) 2-(4-Fluorophenyl)-3-(pyrimidin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD To a suspension of 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** (100 mg) in methanol (2 ml) was added 10% methanolic hydrogen chloride (0.5 ml). The resulting clear solution was concentrated. . . the solution was concentrated in vacuo. The residue was crystallized from a mixture of ethanol and diethyl ether to give 2-(4-fluorophenyl)-3-(pyridin-4-yl)4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** dihydrochloride (100 mg).

DETD (1) 2-(4-Methylthiophenyl)-3-(pyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine**

DETD (2) 2-(4-Fluorophenyl)-3-(2-fluoropyridin-4-yl)pyrazolo-**1,5**-a]**pyrimidine**

DETD (3) 2-(4-Fluorophenyl)-3-(3-methylpyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine**

DETD (4)3-(4-Fluorophenyl)-2-(pyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine**

DETD (5) 2-(4-Fluorophenyl)-3-(pyridin-2-yl)pyrazolo[**1,5**-a]**pyrimidine**

DETD (6) 2- (4-Fluorophenyl) - 3- (pyridin- 3-yl) pyrazolo [**1,5**-a] **pyrimidine**

DETD (1) 3-(4-Fluorophenyl)-2-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD (2) 2-(4-Methylthiophenyl)- 3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD (3) 2- (4-Fluorophenyl) -3- (2-fluoropyridin-4-yl) -4,5,6,7-tetrahydropyrazolo [**1,5**-a] **pyrimidine**

DETD (4) 2-(4-Fluorophenyl)-3-(3-methylpyridin-4-yl) -4,5,6,7-tetrahydropyrazolo [**1,5** -a] **pyrimidine**

DETD (5) 2-(4-Fluorophenyl)-3-(2-methylpyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD (6) 2-(4-Fluorophenyl)-3-(pyridin-2-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD (7) 2-(4-Fluorophenyl)-3-(pyridin-3-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD 2-(4-Fluorophenyl)-4-methyl-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine**

DETD . . . aqueous solution was neutralized with diluted hydrochloric acid. The separated solid was collected, washed with water and dried to give 4,5-dihydro-3-(4-fluorophenyl)-5-oxo-2-(pyridin-4-yl)pyrazolo[**1,5**-a]**pyrimidine** (62 mg).

DETD . . . neutralized with an aqueous saturated sodium bicarbonate solution. The separated solid was collected, washed with water and dried to give 2-(4-fluorophenyl)-5-oxo-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** (750 mg).

DETD . . . of sodium hydride (60% dispersion in mineral oil, 35 mg) in dry N,N-dimethylformamide (5 ml) was added a solution of 2-(4-fluorophenyl)-5-oxo-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** (250 mg) in dry N,N-dimethylformamide (3 ml) dropwise under ice cooling. The mixture was stirred for 30 minutes and to. . . silica gel and the obtained crude solid was recrystallized from a mixture of dichloromethane and diisopropyl ether to give 2-(4-flurorphenyl-4-methyl-5-oxo-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5**-a]**pyrimidine** (180 mg).

DETD To a solution of 2-(4-methylthiophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1**,**5**-a]**pyrimidine** (190 mg) in dichloromethane (6 ml) was added m-chloroperbenzoic acid (127 mg) under ice cooling. The mixture was stirred at. . . chromatography on silica gel and the obtained crude solid was recrystallized from a mixture of 2-propanol and ether to give 2-(4-methylsulfinylphenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1**,**5**-a]**pyrimidine** (168 mg).

DETD To a solution of 2-(4-methylthiophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1**,**5**-a]**pyrimidine** (190 mg) in dichloromethane (6 ml) was added m-chloroperbenzoic acid (318 mg) under ice cooling. The mixture was stirred at. . . chromatography on silica gel and the obtained crude solid was recrystallized from a mixture of 2-propanol and ether to give 2-(4-methylsulfonylphenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazoto[**1**,**5**-a]**pyrimidine** (63 mg).

DETD To a solution of 2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[**1**,**5**-a]**pyrimidine** (480 mg) in dry tetrahydrofuran (15 ml) was added acetyl chloride (0.89 ml) dropwise under ice cooling. The mixture was. . . washed with brine, dried and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give 3-(1-acetyl-1,2-dihydro-2-methylpyridin-4-Yl)-2-(4-fluorophenyl)pyrazolo[**1**,**5**-a]**pyrimidine** (327 mg).

DETD A mixture of 3-(1-acetyl-1,2-dihydro-2-methylpyridin-4-yl)-2-(4-fluorophenyl)pyrazolo[**1**,**5**-a]**pyrimidine** (315 mg) and sulfur (146 mg) in decaline (3 ml) was stirred at 190.degree. C. for 2 hours. The reaction mixture was cooled and purified by column chromatography on silica gel to give 2-(4-fluorophenyl)-3-(2-methylpyridin-4-yl)pyrazolo[**1**,**5**-a]**pyrimidine** (135 mg) as crystals.

DETD A mixture of 3-(4-fluorophenyl)-2-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1**,**5**-a]**pyrimidine** (100 mg), triethylamine (0.4 ml) and acetic anhydride (0.2 ml) in dry 1,2-dichloroethane (3 ml) was refluxed for 2 days.. . . residue was purified by column chromatography on silica gel and the obtained oil was crystallized from diisopropyl ether to give 4-acetyl-3-(4-fluorophenyl)-2-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1**,**5**-a]**pyrimidine** (60 mg).

DETD 2-(4-Fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1**,**5**-a]**pyrimidine** dihydrochloride (183 mg) was dissolved in hot aqueous isopropyl alcohol solution (5.5 ml). The solution was cooled and the separated solid was collected, washed with isopropyl alcohol and dried to give 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1**,**5**-a]**pyrimidine** hydrochloride (82 mg).

DETD To a suspension of 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1**,**5**-a]**pyrimidine** (250 mg) in ethanol (3.5 ml) was added 1N hydrochloric acid (0.85 ml). The resulting clear solution was concentrated in. . . mixture of methanol (0.5 ml) and ethyl acetate (3 ml) and recrystallized from an aqueous isopropyl alcohol solution to give 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1**,**5**-a]**pyrimidine** hydrochloride (233 mg).

DETD . . . The residue was purified by column chromatography on silica gel and the obtained oil was crystallized from methanol to give 5,7-diphenyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[**1**,**5**-a]**pyrimidine** (250 mg).

DETD . . . chromatography on silica gel and the obtained oil was crystallized from a mixture of ethyl acetate and hexane to give 6,7-dihydro-2-(4-fluorophenyl)-3-(pyridin-4-yl)-5,7,7-trimethylpyrazolo[**1**,**5**-a]**pyrimidine** (83 mg).

DETD . . . 1N-hydrochloric acid (4 ml) and water (6 ml). The separated solid was collected, washed with water and dried to give 5,7-dihydroxy-2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[**1,5-a**]**pyrimidine** (210 mg).

DETD . . . the reaction mixture was diluted with ethanol to crystallize. The crude crystalline was collected and washed with ethanol to give 4,7-dihydro-2-(4-fluorophenyl)-5-methyl-7-oxo-3-(pyridin-4-yl)pyrazolo[**1,5-a**]**pyrimidine** (104 mg).

DETD . . . refluxed for 1 hour. The reaction mixture was concentrated in vacuo and the residue was crystallized from ethanol to give 7-amino-6-cyano-2-(4-fluorophenyl)-3-(pyridin-4-yl)pyrazolo[**1,5-a**]**pyrimidine** (77 mg).

DETD . . . (10 ml) was refluxed for 3 hours. After cooling, the crude crystalline was obtained and washed with ethanol to give 4,7-dihydro-6-ethoxycarbonyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)-7-oxopyrazolo[**1,5-a**]**pyrimidine** (1.23 g).

DETD To a mixture of 4,7-dihydro-6-ethoxycarbonyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)-7-oxopyrazolo[**1,5-a**]**pyrimidine** (100 mg) in tetrahydrofuran (4 ml) was added lithium borohydride (2 mole in tetrahydrofuran, 0.26 ml) at room temperature and. . . acetate. The extracts were washed with brine, dried and concentrated in vacuo. The residue was crystallized from ethanol to give 6-ethoxycarbonyl-2-(4-fluorophenyl)-7-oxo-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5-a**]**pyrimidine** (40 mg).

DETD A mixture of 4,7-dihydro-6-ethoxycarbonyl-2- (4-fluorophenyl)-3-(pyridin-4-yl)-7-oxopyrazolo [**1,5-a**] **pyrimidine** (946 mg) in sulfuric acid (40% in water, 5 ml) was refluxed for 2 hours. After cooling, the pH of. . . 5 with an aqueous saturated sodium bicarbonate solution. The crude crystalline was obtained and washed with hot ethanol to give 4,7-dihydro-6-carboxy-2-(4-fluorophenyl)-3-(pyridin-4-yl)-7-oxopyrazolo[**1,5-a**]**pyrimidine** (275 mg).

DETD . . . 1N-hydrochloric acid (2 ml) and water (5 ml). The separated solid was collected, washed with water and dried to give 7-amino-2-(4-fluorophenyl)-5-hydroxy-3-(pyridin-4-yl)pyrazolo[**1,5-a**]**pyrimidine** (270 mg).

DETD 4-Acetyl-2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5-a**]**pyrimidine**

CLM What is claimed is:
6. A compound of claim 5, which is 2-(4-fluorophenyl)-3-(pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[**1,5-a**]**pyrimidine** or its hydrochloride.

L10 ANSWER 24 OF 25 USPATFULL

PI US 4912104 19900327 <--

SUMM . . . analgesic, antipyretic, anti-allergic and anti-psoriatic actions on mammals including man, and are useful as ameliorating and therapeutic agents for chronic **rheumatoid arthritis**, lumbago, neck-shoulder-arm syndrome, psoriasis, etc. The compounds (I) have a liver-protecting action against hepatic injury due to various causes, and. . .

SUMM . . . symptoms, subjects, routes of administration, etc. In the case of oral administration to, for example, human adults suffering from chronic **rheumatoid arthritis** or hepatic injury, it is usually preferable to administer the pharmaceutically effective component [compound (I)] in a single dose in. . .

DETD 6-Isobutyl-1-propionyl-8-propyl-2,3-dihydro-1H-imidazo[2',1':**5,1**]pyrazolo[3,4-**pyrimidine**-7,9(6H,8H)-dione

DETD When a compound(I) of the present invention is intended for use as a therapeutic agent of chronic **rheumatoid arthritis**,

lumbago, neck-shoulder-arm syndrome, liver disease or psoriasis, etc., the compound can be formulated into, for example, tablets or capsules having. . .

CLM What is claimed is:

16. A compound according to claim 1, which is 6,8-diallyl-1-propionyl-2,3-dihydro-1H-imidazo[2',1':5,1]pyrazolo[3,4-**pyrimidine**-7,9(6H,8H)-dione.

21. A method for treatment or amelioration of chronic **rheumatoid arthritis**, lumbago, or neck-shoulder-arm syndrome in a mammal, which comprises administering to said mammal an effective amount of a compound as. . .

L10 ANSWER 25 OF 25 USPATFULL

PI US 4482555 19841113 <--

SUMM 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(3-pyridyl)-carboxamide;

SUMM 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

SUMM 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

SUMM 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyrimidinyl)-carboxamide;

SUMM 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methoxy-3-pyridyl)-carboxamide;

SUMM 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyrimidinyl)-carboxamide;

SUMM 3,5-dimethyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 5-ethyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-(3-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-(3-chloro-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-(4-chloro-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-(4-amino-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-(4-acetylamino-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

SUMM 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

SUMM 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

SUMM 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

SUMM 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]

pyrimidine-6-N-(2-thiazolyl)-carboxamide;

SUMM 1-benzyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-piperidino-ethyl)-carboxamide;

SUMM 1-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-ethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

SUMM 1-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-benzothiazolyl)-carboxamide;

SUMM 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

SUMM 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-benzothiazolyl)-carboxamide;

SUMM 1-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-piperidino-ethyl)-carboxamide;

SUMM 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

SUMM 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

SUMM 1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-carboxylic acid;

SUMM 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-carboxylic acid;

SUMM 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-carboxylic acid; and

SUMM 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-carboxylic acid; and the pharmaceutically acceptable salts thereof.

SUMM Therefore the compounds of the invention may be used in therapy to treat pains and inflammatory processes, for example, **rheumatoid arthritis** and osteoarthrosis.

SUMM TABLE I

Compound	Antiinflammatory activity carrageenin induced oedema
1-phenyl-7-oxo-1H,7H--pyrazolo[**1,5**-a]**pyrimidine**-6-N--(2-pyridyl)-carboxamide	ED.sub.25 = 16 mg/kg
5-methyl-1-phenyl-7-oxo-1H,7H--pyrazolo[1,5-a]pyrimidine-6-N--(2-pyridyl)-carboxamide	ED.sub.25 = 9.8 mg/kg

SUMM For example, the compound of this invention 1-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide (internal code FCE 23081) was tested versus

the compound of the above prior art 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester (internal code SR 5444/50) according to the carrageenin and RPAR tests described above, and the following results. . .

SUMM . . . compounds of the invention can be used safely in medicine. For example, the approximate acute toxicity (LD.sub.50) of the compounds 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid and 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide in the mouse, determined by single administration of increasing doses and measured on the seventh day after the treatment, is. . .

DETD . . . with charcoal: neutralization with 35% NaOH gave a precipitate which was filtered and washed with water. Washing with hexane gave 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 187.degree.-190.degree. C. (24.2 g), which was hydrolized by heating with a mixture 1:1 of 37% HCl:acetic. . . with 35% NaOH and the precipitate was filtered and washed with water: crystallization from isopropyl alcohol gave 9.7 g of 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid m.p. 185.degree.-190.degree. C. dec., N.M.R. (DMSO-d.sub.6) .delta. p.p.m.: 6.94 (d) (1H, C-3 proton), 7.59 (s) (5H, phenyl protons), 8.74. . .

DETD 2-chloro-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 196.degree. C.;

DETD 1-(2-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 1-(3-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 1-(2-methoxy-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 1-(4-methoxy-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 1-(4-nitro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 240.degree.-250.degree. C.;

DETD 1-(4-fluoro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 215.degree.-220.degree. C. dec.;

DETD 1-(2-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 1-(3-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 200.degree.-205.degree. C.;

DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 181.degree.-183.degree. C.;

DETD 1-(3-trifluoromethyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 181.degree.-183.degree. C.;

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 182.degree.-185.degree. C.;

DETD 1-(3-chloro-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 1-(4-chloro-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 1-(4-chloro-phenyl)-2-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 3-methyl-1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 2-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 160.degree.-163.degree. C.;

DETD 3-bromo-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 185.degree.-187.degree. C.;

DETD 1-(2-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 1-(3-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, m.p. 185.degree.-188.degree. C. dec.;

DETD 1-(2-methoxy-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 1-(3-methoxy-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 1-(4-methoxy-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 1-(4-fluoro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 1-(2-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 1-(3-chloro-phenyl)-7-oxo-1H-7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 1-(3-trifluoromethyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 2-chloro-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 3-methyl-1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 1-(3-chloro-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 1-(4-chloro-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid; and

DETD 1-(4-methoxy-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid.

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 172.degree.-173.degree. C.;

DETD 5-methyl-1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 1-(3-chloro-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 1-(4-chloro-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 1-(4-fluoro-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 175.degree.-177.degree. C.;

DETD 1,5-diphenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester;

DETD 5-ethyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid;

DETD 5-ethyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester, m.p. 119.degree.-120.degree. C.;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid;
DETD 5-methyl-1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5
-a]**pyrimidine**-6-carboxylic acid;
DETD 1-(3-chloro-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5
-a]**pyrimidine**-6-carboxylic acid;
DETD 1-(4-chloro-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5
-a]**pyrimidine**-6-carboxylic acid;
DETD 1-(4-fluoro-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5
-a]**pyrimidine**-6-carboxylic acid; and
DETD 1,5-diphenyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid.
DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid, ethyl ester, m.p.
138.degree.-139.degree. C.;
DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid, ethyl ester, m.p.
203.degree.-207.degree. C.;
DETD 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid, ethyl ester;
DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid, ethyl ester, m.p.
103.degree.-104.degree. C.;
DETD 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid, ethyl ester;
DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid;
DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid;
DETD 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid;
DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid; and
DETD 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid.
DETD . . . with 35% NaOH gave a precipitate which was filtered and washed with water. Crystallization from methanol gave 6 g of 1-benzyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid, ethyl ester, m.p.
172.degree.-173.degree. C., which was hydrolized by heating with a mixture 1:1 of 37% HCl:acetic acid (300. . . . with 35% NaOH and the precipitate was filtered and washed with water: crystallization from isopropyl alcohol gave 9.7 g of 1-benzyl-7-oxo-1H,7H-pyrazolo[1
,5-a]**pyrimidine**-6-carboxylic acid, m.p.
198.degree.-199.degree. C.
DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid, ethyl ester;
DETD 1-benzyl-5-ethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid, ethyl ester;
DETD 1-benzyl-5-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid, ethyl ester;
DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid;
DETD 1-benzyl-5-ethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid; and
DETD 1-benzyl-5-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid.
DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-carboxylic acid (3 g), was reacted with thionyl chloride (2.8 g) in dioxane (70 ml) at the reflux temperature for 1 hour, then the mixture was evaporated in vacuo to dryness. The crude 6-chlorocarbonyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5

-a]**pyrimidine** was suspended in dioxane (60 ml) and reacted under stirring at room temperature for 30 minutes with methylamine (3.75 g). The precipitate was filtered and washed with water until neutral: crystallization from isopropyl alcohol gave 1.7 g of 1-phenyl-7-oxo-1H,7-pyrazolo[1,5-a] **pyrimidine**-6-N-methyl-carboxamide, m.p. 244.degree.-246.degree. C., N.M.R. (CDCl.sub.3) .delta. p.p.m.: 2.92 (d) (3H, --CH.sub.3), 6.73 (d) (1H, C-3 proton), 7.37-7.75 (m) (5H, phenyl. . .

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-carboxamide, m.p. 265.degree.-270.degree. C. dec.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-ethyl-carboxamide, m.p. 225.degree.-230.degree. C. dec.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N,N-diethyl-carboxamide, m.p. 146.degree.-147.degree. C.;

DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-ethyl-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-isopropyl-carboxamide, m.p. 220.degree.-225.degree. C. dec.;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-phenyl-carboxamide;

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-phenyl-carboxamide;

DETD 2-chloro-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-phenyl-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-phenyl-carboxamide, m.p. 245.degree.-247.degree. C.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(3-pyridyl)-carboxamide, m.p. 207.degree.-210.degree. C.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(4-methyl-phenyl)-carboxamide;

DETD 1-(3-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-methyl-carboxamide;

DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-methyl-carboxamide;

DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-ethyl-carboxamide;

DETD 1-(4-chloro-phenyl)-7-oxo-1H,7-pyrazolo[1,5-a] **pyrimidine**-6-N-isopropyl-carboxamide;

DETD 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-methyl-carboxamide;

DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-methyl-carboxamide;

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-methyl-carboxamide;

DETD 1-(3-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6N-phenyl-carboxamide;

DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-phenyl-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(4-chloro-phenyl)-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methoxy-3-pyridyl)-carboxamide;

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-ethyl-carboxamide;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-methyl-carboxamide;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]

pyrimidine-6-N-ethyl-carboxamide;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N,N-diethyl-carboxamide;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-isopropyl-carboxamide;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4-chloro-phenyl)-carboxamide;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4-methoxy-phenyl)-carboxamide; and

DETD 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-ethyl-carboxamide.

DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N,N-diethyl-carboxamide;

DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-ethyl-carboxamide;

DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-isopropyl-carboxamide;

DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4-methyl-phenyl)-carboxamide;

DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4-chloro-phenyl)-carboxamide;

DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-methyl-carboxamide;

DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-ethyl-carboxamide;

DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N,N-diethyl-carboxamide;

DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-isopropyl-carboxamide;

DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4-chloro-phenyl)-carboxamide;

DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4-methoxy-phenyl)-carboxamide;

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-isopropyl-carboxamide;

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N,N-diethyl-carboxamide;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-methyl-carboxamide;

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-methyl-carboxamide;

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-ethyl-carboxamide;

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4-chloro-phenyl)-carboxamide;

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4-methoxy-phenyl)-carboxamide;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-isopropyl-carboxamide;

DETD 1-ethyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-methyl-carboxamide;

DETD 1-ethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-isopropyl-carboxamide;

DETD 1-ethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-ethyl-carboxamide;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-ethyl-carboxamide;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N,N-diethyl-carboxamide;

DETD 1-ethyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-ethyl-carboxamide;

DETD 1-ethyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]

pyrimidine-6-N-isopropyl-carboxamide;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(4-chloro-phenyl)-carboxamide;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(4-methoxy-phenyl)-carboxamide;

DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-isopropyl-carboxamide;

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-isopropyl-carboxamide;

DETD 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-isopropyl-carboxamide;

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-methyl-carboxamide;

DETD 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-methyl-carboxamide;

DETD 5-methyl-1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-methyl-carboxamide;

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-ethyl-carboxamide;

DETD 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-ethyl-carboxamide;

DETD 5-methyl-1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-ethyl-carboxamide;

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-isopropyl-carboxamide;

DETD 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-isopropyl-carboxamide; and

DETD 5-methyl-1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-isopropyl-carboxamide.

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid (1.2 g) was reacted with thionyl chloride (0.8 ml) in dioxane (30 ml) at the reflux temperature for 3. . . Na.sub.2 CO.sub.3 the precipitate was extracted with ethyl acetate: evaporation to dryness and crystallization from chloroformethanol gave 0.7 g of 1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid, 2-(diethylamino)-ethyl ester, m.p. 127.degree.-130.degree. C.

DETD 1-(4-fluoro-phenyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid, 2-(diethylamino)-ethyl ester;

DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid, 2-(diethylamino)-ethyl ester;

DETD 1-(3-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid, 2-(diethylamino)-ethyl ester;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid, 2-(diethylamino)-ethyl ester, m.p. 153.degree.-154.degree. C.;

DETD 1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid, 2-(diethylamino)-ethyl ester;

DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid, 2-(diethylamino)-ethyl ester;

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid, 2-(diethylamino)-ethyl ester;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid, 2-(diethylamino)-ethyl ester;

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid, 2-(diethylamino)-ethyl ester; and

DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid, 2-(diethylamino)-ethyl ester.

DETD 6-chlorocarbonyl-1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**
-a]**pyrimidine** (2.7 g) was reacted with N-(2-amino-ethyl)-piperidine (2.5 g) in dioxane (55 ml) at room temperature for 30 minutes. After evaporation. . . over a SiO.sub.2 column using

CHCl.sub.3 :CH.sub.3 OH=85:15 as eluent. Crystallization from CH.sub.2 Cl.sub.2 -isopropyl ether gave 2.1 g of 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-piperidino-ethyl)-carboxamide, m.p. 136.degree.-138.degree. C.

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-morpholino-ethyl)-carboxamide, m.p. 179.degree.-180.degree. C.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-[2-(pyrrolidin-1-yl)-ethyl]-carboxamide, m.p. 145.degree.-148.degree. C.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-[2-(N,N-diethylamino)-ethyl]-carboxamide, m.p. 135.degree.-137.degree. C.;

DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-piperidino-ethyl)-carboxamide;

DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-[2-(N,N-diethylamino)-ethyl]-carboxamide;

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-piperidino-ethyl)-carboxamide;

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-[2-(N,N-diethylamino)-ethyl]-carboxamide;

DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-piperidino-ethyl)-carboxamide;

DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-[2-(N,N-diethylamino)-ethyl]-carboxamide;

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-piperidino-ethyl)-carboxamide;

DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-morpholino-ethyl)-carboxamide;

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-[2-(N,N-diethylamino)-ethyl]-carboxamide;

DETD 5-methyl-1-phenyl-7-oxo-1H-7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-piperidino-ethyl)-carboxamide;

DETD 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-piperidino-ethyl)-carboxamide; and

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-piperidino-ethyl)-carboxamide.

DETD 6-chlorocarbonyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine** (2.7 g), prepared according to Example 5, was reacted with piperidine (1.65 g) in dioxane (45 ml) at room temperature.

. .

DETD Crystallization from CH.sub.2 Cl.sub.2 -isopropyl ether gave 2.35 g of 1-phenyl-6-piperidinocarbonyl-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one, m.p. 160.degree.-161.degree. C.

DETD 6-(4-methyl-piperazin-1-yl)carbonyl-1-phenyl-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one, m.p. 185.degree.-186.degree. C.;

DETD 6-morpholinocarbonyl-1-phenyl-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one, m.p. 150.degree.-152.degree. C.;

DETD 6-morpholinocarbonyl-1-(3-pyridyl)-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 6-(4-methyl-piperazin-1-yl)carbonyl-1-(3-pyridyl)-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 6-piperidinocarbonyl-1-(3-pyridyl)-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 5-methyl-6-(4-methyl-piperazin-1-yl)carbonyl-1-phenyl-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 6-piperidinocarbonyl-1-(2-pyridyl)-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 5-methyl-6-morpholinocarbonyl-1-phenyl-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 5-methyl-6-morpholinocarbonyl-1-(3-pyridyl)-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 5-methyl-6-(4-methyl-piperazin-1-yl)carbonyl-1-(3-pyridyl)-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 5-methyl-6-piperidinocarbonyl-1-(3-pyridyl)-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 1-benzyl-6-morpholinocarbonyl-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 1-benzyl-6-(4-methyl-piperazin-1-yl)carbonyl-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 1-methyl-6-morpholinocarbonyl-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 1-methyl-6-(4-methyl-piperazin-1-yl)carbonyl-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 6-morpholinocarbonyl-1-(2-pyridyl)-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 6-(4-methyl-piperazin-1-yl)carbonyl-1-(2-pyridyl)-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 5-methyl-6-piperidinocarbonyl-1-(2-pyridyl)-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one;

DETD 5-methyl-6-morpholinocarbonyl-1-(2-pyridyl)-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one; and

DETD 5-methyl-6-(4-methyl-piperazin-1-yl)-1-(2-pyridyl)-1H,7H-pyrazolo[1,5-a]**pyrimidine**-7-one.

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid (5.1 g) was reacted with 2-amino-thiazole (4 g) in polyphosphoric acid (90 g: 47.7 g of H.sub.3 PO.sub.4 and. . . neutralization with 35% NaOH, the precipitate was filtered and washed with water: crystallization from CHCl.sub.3 -methanol gave 4.5 g of 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-thiazolyl)-carboxamide, m.p. 245.degree.-247.degree. C. dec., N.M.R. (CDCl.sub.3) .delta. p.p.m.: 6.72 (d) (1H, C-3 proton), 6.84 (d) (1H, C-5 thiazolyl proton), 7.4-7.7. . .

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 207.degree.-210.degree. C. dec.;

DETD 5-ethyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-thiazolyl)-carboxamide; and

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 184.degree.-187.degree. C.

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-carboxylic acid, ethyl ester (17 g) was reacted with 2-amino-pyridine (10.8 g) in polyphosphoric acid (270 g) under stirring at 120.degree.. . . with 35% NaOH, the precipitate was filtered and washed with water: crystallization from CH.sub.2 Cl.sub.2 -methanol gave 14 g of 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 186.degree.-187.degree. C., N.M.R. (CDCl.sub.3) .delta. p.p.m.: 2.88 (s) (3H, --CH.sub.3), 6.62 (d) (1H, C-3 proton), 6.99 (m) (1H, C-5. . .

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 207.degree.-210.degree. C.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide, m.p. 260.degree. C. dec.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(5-methyl-2-pyridyl)-carboxamide, m.p. 268.degree.-270.degree. C.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(4-methyl-2-pyridyl)-carboxamide, m.p. 210.degree.-215.degree. C. dec.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-pyrazinyl-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide, m.p. 235.degree.-240.degree. C. dec.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-bromo-2-pyridyl)-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-hydroxy-2-pyridyl)-carboxamide, m.p. 280.degree.-290.degree. C. dec.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(3-methyl-2-pyridyl)-carboxamide, m.p. 252.degree.-254.degree. C.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methoxy-2-benzothiazolyl)-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(4-methyl-2-thiazolyl)-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-benzothiazolyl)-carboxamide, m.p. 245.degree.-250.degree. C.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(4-phenyl-2-thiazolyl)-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(1-methyl-3-pyrazolyl)-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(1-phenyl-3-pyrazolyl)-carboxamide, m.p. 248.degree.-252.degree. C.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-thiazolyl)-carboxamide;

DETD 1-(4-methoxy-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1-(4-methoxy-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyrimidinyl)-carboxamide, m.p. 200.degree.-205.degree. C. dec.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(3,5-dichloro-2-pyridyl)-carboxamide, m.p. 305.degree.-310.degree. C. dec.;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(4-pyridyl)-carboxamide, m.p. 270.degree.-275.degree. C. dec.;

DETD 2-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 225.degree.-230.degree. C. dec.;

DETD 1-(4-methoxy-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

DETD 1-(4-methoxy-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;

DETD 1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

DETD 1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;

DETD 1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 209.degree.-213.degree. C. dec.;

DETD 1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]

pyrimidine-6-N-(6-methyl-2-pyridyl)-carboxamide;
DETD 1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide;
DETD 1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-benzothiazolyl)-carboxamide;
DETD 1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(4-methyl-2-thiazolyl)-carboxamide;
DETD 1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(5-chloro-2-thiazolyl)-carboxamide;
DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide, m.p.
254.degree.-257.degree. C.;
DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(6-methyl-2-pyridyl)-carboxamide;
DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide;
DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-benzothiazolyl)-carboxamide;
DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(4-methyl-2-thiazolyl)-carboxamide;
DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(5-chloro-2-thiazolyl)-carboxamide;
DETD 1-(4-fluoro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide, m.p.
202.degree.-210.degree. C. dec.;
DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(5-chloro-2-pyridyl)-carboxamide;
DETD 1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;
DETD 1-(4-nitro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide, m.p.
305.degree.-310.degree. C.;
DETD 1-(4-fluoro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(5-chloro-2-pyridyl)-carboxamide;
DETD 1-(4-fluoro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;
DETD 1-(4-fluoro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(6-methyl-2-pyridyl)-carboxamide;
DETD 1-(4-fluoro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide;
DETD 1-(4-fluoro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-benzothiazolyl)-carboxamide;
DETD 1-(4-fluoro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(4-methyl-2-thiazolyl)-carboxamide;
DETD 1-(4-fluoro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(5-chloro-2-thiazolyl)-carboxamide;
DETD 1-(3-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide, m.p.
284.degree.-286.degree. C.;
DETD 1-(3-trifluoromethyl-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**
-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p.
246.degree.-251.degree. C.;
DETD 1-(3-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide;
DETD 1-(3-trifluoromethyl-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**
-a]**pyrimidine**-6-N-(2-thiazolyl)-carboxamide;
DETD 1-(2-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide;
DETD 1-(2-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide;
DETD 1-(3-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide;

DETD 1-(3-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 274.degree.-277.degree. C.;

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-benzothiazolyl)-carboxamide;

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(4-methyl-2-thiazolyl)-carboxamide;

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-thiazolyl)-carboxamide;

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;

DETD 3-methyl-1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 2-chloro-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 275.degree.-278.degree. C.;

DETD 2-chloro-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 2-chloro-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 2-chloro-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

DETD 1-(4-fluoro-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 252.degree.-255.degree. C.;

DETD 1-(4-chloro-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1-(3-chloro-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 3-methyl-1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1-(4-fluoro-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 1-(4-chloro-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 1-(3-chloro-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 3-methyl-1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 1-(4-fluoro-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 1-(4-chloro-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 1-(4-methoxy-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 1,5-diphenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 5-ethyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1-(4-chloro-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5 -a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1-(3-chloro-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5

-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 5-methyl-1-(4-methyl-phenyl)-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(2-pyrimidinyl)-carboxamide; and

DETD 3,5-dimethyl-1-phenyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide.

DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-carboxylic acid, ethyl ester (3.5 g) was reacted with 2-amino-pyridine (5.2 g) in polyphosphoric acid (87 g) under stirring at 120.degree.. . . and neutralization with 35% NaOH, the precipitate was filtered and washed with water: crystallization from dimethylformamide gave 1.5 g of 1-benzyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 337.degree.-340.degree. C.

DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[B **1**,**5**-a]**pyrimidine**-6-N-(3-pyridyl)-carboxamide;

DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(3-pyridyl)-carboxamide; and

DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide.

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-carboxylic acid, ethyl ester (3.4 g) was reacted with 2-amino-pyrimidine (2.9 g) in polyphosphoric acid (51 g) under stirring at 110.degree.. . . with 35% NaOH the precipitate was filtered and washed with water: crystallization from CH.sub.2 Cl.sub.2 /ethanol gave 2.6 g of 1-methyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 222.degree.-226.degree. C., N.M.R. (CDCl.sub.3 -CF.sub.3 COOD) .delta. p.p.m.: 4.71 (s) (3H, CH.sub.3), 6.97 (d) (1H, C-3 proton), 7.80 (m).

DETD 1-ethyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1-tert.butyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1-tert.butyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 212.degree.-214.degree. C.;

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(3-pyridyl)-carboxamide;

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide, m.p. 270.degree.-273.degree. C. (dec.);

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(3-pyridyl)-carboxamide;

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide, m.p. 225.degree.-227.degree. C.;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[**1**,**5**-a]**pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide, m.p.

256.degree.-259.degree. C.;
DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(6-methyl-2-pyridyl)-carboxamide, m.p.
220.degree.-221.degree. C.
DETD 1-ethyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(6-methyl-2-pyridyl)-carboxamide;
DETD 1-ethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(5-chloro-2-pyridyl)-carboxamide;
DETD 1-tert.butyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(6-methyl-2-pyridyl)-carboxamide;
DETD 1-ethyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide;
DETD 1-ethyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(5-chloro-2-pyridyl)-carboxamide; and
DETD 1-tert.butyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(5-chloro-2-pyridyl)-carboxamide.
DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide;
DETD 1-benzyl-7-oxo-1H-7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-benzothiazolyl)-carboxamide;
DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4-methyl-2-thiazolyl)-carboxamide;
DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(5-chloro-2-thiazolyl)-carboxamide;
DETD 1-benzyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;
DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide, m.p.
265.degree.-268.degree. C. (dec.);
DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-benzothiazolyl)-carboxamide, m.p.
293.degree.-298.degree. C. (dec.);
DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4-methyl-2-thiazolyl)-carboxamide;
DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(5-chloro-2-thiazolyl)-carboxamide;
DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;
DETD 1-ethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide
DETD 1-tert.butyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;
DETD 1-tert.butyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide;
DETD 1-tert.butyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-benzothiazolyl)-carboxamide;
DETD 1-tert.butyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(4-methyl-2-thiazolyl)-carboxamide;
DETD 1-tert.butyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(5-chloro-2-thiazolyl)-carboxamide;
DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide;
DETD 1-tert.butyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide;
DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide, m.p.
243.degree.-245.degree. C.;
DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(5-chloro-thiazolyl)-carboxamide;
DETD 1-ethyl-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(B 5-chloro-2-thiazolyl)-carboxamide;
DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[1,5-a]

pyrimidine-6-N-(5-chloro-2-thiazolyl)-carboxamide;
DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;
DETD 1-ethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(4-methyl-2-thiazolyl)-carboxamide;
DETD 1-ethyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;
DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;
DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(4-methyl-2-thiazolyl)-carboxamide;
DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(4-methyl-2-thiazolyl)-carboxamide;
DETD 1-tert.butyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(4-methyl-2-thiazolyl)-carboxamide;
DETD 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(2-benzothiazolyl)-carboxamide;
DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(2-benzothiazolyl)-carboxamide;
DETD 1-tert.butyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(2-benzothiazolyl)-carboxamide;
DETD 1-ethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(4,5-dimethyl-2-thiazolyl)-carboxamide;
DETD 1-ethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(2-benzothiazolyl)-carboxamide;
DETD 1-ethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(5-chloro-2-thiazolyl)-carboxamide;
DETD 1-ethyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide;
DETD 1-ethyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(2-benzothiazolyl)-carboxamide; and
DETD 1-ethyl-5-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(4-methyl-2-thiazolyl)-carboxamide.
DETD . . . pyridine (10 ml) was reacted with PCl.sub.3 (1.24 g) at 55.degree. C. for 30 minutes: after cooling at 20.degree. C. 1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-carboxylic acid (4 g) was added and the mixture was kept to the reflux temperature for 30 minutes. After cooling, dilution. . . and purified over a SiO.sub.2 column using ethyl acetate: methanol 98:2 as eluent. Crystallization from methanol gave 2 g of 1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide, m.p. 207.degree.-210.degree. C. dec., N.M.R. (CDCl.sub.3) .delta. p.p.m: 6.74 (d) (1H, C-3 proton), 7.04 (m) (1H, C-5 pyridyl proton), 7.3-7.9. . .
DETD 3-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide, m.p. 274.degree.-277.degree. C.; and
DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide, m.p. 184.degree.-187.degree. C.
DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide, m.p. 202.degree.-204.degree. C.;
DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide, m.p. 218.degree.-220.degree. C.;
DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(6-methyl-2-pyridyl)-carboxamide, m.p. 212.degree.-214.degree. C.;
DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]
pyrimidine-6-N-(2-benzothiazolyl)-carboxamide;
DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]

pyrimidine-6-N-(2-pyridyl)-carboxamide; m.p. 291.degree.-293.degree. C.(dec.);

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-benzothiazolyl)-carboxamide;

DETD 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-benzothiazolyl)-carboxamide;

DETD 3-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 3-methyl-1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 183.degree.-187.degree. C. (dec.);

DETD 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 3-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 3-methyl-1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 3-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 3-methyl-1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide;

DETD 3-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-benzothiazolyl)-carboxamide;

DETD 3-methyl-1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-benzothiazolyl)-carboxamide;

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-benzothiazolyl)-carboxamide;

DETD 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-benzothiazolyl)-carboxamide;

DETD 2-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 2-methyl-1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(3-pyridyl)-carboxamide;

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(3-pyridyl)-carboxamide;

DETD 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(3-pyridyl)-carboxamide;

DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]

pyrimidine-6-N-(5-chloro-2-pyridyl)-carboxamide, m.p. 292.degree.-294.degree. C. (dec.);

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;

DETD 1-(4-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide; and

DETD 5-methyl-1-(4-pyridyl)-7-oxo-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide.

DETD 1-(4-nitro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide (4.1 g), prepared according to Example 11, was reacted with SnCl.sub.2.2H.sub.2 O (25 g) in 37% HCl (15 ml) and. . . the product was filtered, washed with water until neutral and then crystallized from CHCl.sub.3 -methanol to give 2.9 g of 1-(4-amino-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 235.degree.-245.degree. C. dec.

DETD 1-(4-amino-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 1-(4-amino-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1-(4-amino-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide; and

DETD 1-(4-amino-phenyl)-2-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide.

DETD 1-(4-amino-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide (2 g), prepared according to Example 17, was reacted with acetic anhydride (2 ml) in dimethylformamide (30 ml) in the. . . 120.degree. C. for 1 hour. After cooling the precipitate was filtered and washed with methanol to give 1.7 g of 1-(4-acetylamino-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, m.p. 327.degree.-332.degree. C.

DETD 1-(4-acetylamino-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(2-thiazolyl)-carboxamide;

DETD 1-(4-acetylamino-phenyl)-3-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;

DETD 1-(4-acetylamino-pheny)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboximide; and

DETD 1-(4-acetylamino-phenyl)-2-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide.

DETD 5-methyl-1-phenyl-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(3-pyrazolyl)-carboxamide;

DETD 5-methyl-1-phenyl-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(1-methyl-3-pyrazolyl)-carboxamide;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(3-pyridyl)-carboxamide;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(6-methoxy-3-pyridyl)-carboxamide;

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(3-pyrazolyl)-carboxamide; m.p. 300.degree.-305.degree. C. (dec.);

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(1-methyl-3-pyrazolyl)-carboxamide;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(1-methyl-3-pyrazolyl)-carboxamide;

DETD 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(3-pyrazolyl)-carboxamide, m.p. 296.degree.-298.degree. C. (dec.);

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a] **pyrimidine**-6-N-(5-bromo-2-pyridyl)-carboxamide, m.p. 255.degree.-260.degree. C. (dec.);

DETD 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]

pyrimidine-6-N-(2-pyrazinyl)-carboxamide;

DETD 1-methyl-7-oxo-1H,7-H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(2-pyrimidinyl)-carboxamide, m.p. 240.degree.-245.degree. C.;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(2-pyrimidinyl)-carboxamide;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(2-pyrazinyl)-carboxamide;

DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(2-pyrimidinyl)-carboxamide;

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(2-pyrimidinyl)-carboxamide;

DETD 1,5-dimethyl-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(3-pyrazolyl)-carboxamide;

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(4-methyl-2-thiazolyl)-carboxamide;

DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(3-pyrazolyl)-carboxamide;

DETD 1-(2-pyridyl-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(1-methyl-3-pyrazolyl)-carboxamide;

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(3-pyrazolyl)-carboxamide;

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(1-methyl-3-pyrazolyl)-carboxamide;

DETD 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(2-pyrazinyl)-carboxamide;

DETD 5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(2-pyrazinyl)-carboxamide;

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(3-pyrazolyl)-carboxamide;

DETD 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(1-methyl-3-pyrazolyl)-carboxamide;

DETD 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(3-pyrazolyl)-carboxamide; and

DETD 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(1-methyl-3-pyrazolyl)-carboxamide.

DETD

Compositions (for 10,000 tablets)

5-methyl-1-phenyl-7-oxo-1H,7H--pyrazolo[**1,5**-a]**pyrimidine**-6-N--(2-pyridyl)-carboxamide	500	g
Lactose	710	g
Corn starch	237.5	g
Talc powder	35.5	g
Magnesium stearate	15	g

DETD 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(2-pyridyl)-carboxamide, lactose and a half of the corn starch are mixed; the mixture is then forced through a sieve of 0.5. . .

CLM What is claimed is:

4. A compound selected from the group consisting of: 1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(3-pyridyl)-carboxamide; 1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide; 1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(6-methyl-2-pyridyl)-carboxamide; 1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide; 1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a] **pyrimidine**-6-N-(2-pyrimidinyl)-carboxamide; 3-methyl-1-phenyl-7-

oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**
-6-N-(2-pyridyl)-carboxamide; 1-phenyl-7-oxo-1H,7H-pyrazolo[1,
5-a]**pyrimidine**-6-N-(6- methoxy-3-pyridyl)-carboxamide;
5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide; 5-methyl-1-phenyl-7-oxo-
1H,7H-pyrazolo[1,5-a]**pyrimidine**
-6-N-(2-pyrimidinyl)-carboxamide; 3,5-dimethyl-1-phenyl-7-oxo-1H,7H-
pyrazolo[1,5-a]**pyrimidine**
-6-N-(2-pyridyl)-carboxamide; 5-ethyl-1-phenyl-7-oxo-1H,7H-pyrazolo[
1,5-a]**pyrimidine**-6-N-(2-pyridyl)-
carboxamide; 1-(3-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,
5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;
1-(3-chloro-phenyl)-5-methyl-7-oxo-1H,7H-pyrazolo[1,5
-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;
1-(4-chloro-phenyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide; 1-(4-chloro-phenyl)-5-
methyl-7-oxo-1H,7H-pyrazolo[1,5-a]**pyrimidine**
-6-N-(2-pyridyl)-carboxamide; 1-(4-amino-phenyl)-7-oxo-1H,7H-pyrazolo[
1,5-a]**pyrimidine**-6-N-(2-pyridyl)-
carboxamide; 1-(4-acetylamino-phenyl)-7-oxo-1H,7H-pyrazolo[1,
5-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide;
1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide; 1-(3-pyridyl)-7-oxo-
1H,7H-pyrazolo[1,5-a]**pyrimidine**
-6-N-(6-methyl-2-pyridyl)-carboxamide; 5-methyl-1-(3-pyridyl)-7-oxo-
1H,7H-pyrazolo[1,5-a]**pyrimidine**
-6-N-(2-pyridyl)-carboxamide; 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[
1,5-a]**pyrimidine**-6-N-(5-chloro-2-pyridyl)-
carboxamide; 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5
-a]**pyrimidine**-6-N-(2-thiazolyl)-carboxamide;
1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(5-chloro-2-pyridyl)-carboxamide;
5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide; 1-benzyl-7-oxo-1H,7H-
pyrazolo[1,5-a]**pyrimidine**
-6-N-(2-pyridyl)-carboxamide; 1-benzyl-5-methyl-7-oxo-1H,7H-pyrazolo[
1,5-a]**pyrimidine**-6-N-(2-pyridyl)-
carboxamide; 1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-piperidino-ethyl)-carboxamide;
1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide; 1-ethyl-7-oxo-1H,7H-
pyrazolo[1,5-a]**pyrimidine**
-6-N-(2-pyridyl)-carboxamide; 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[
1,5-a]**pyrimidine**-6-N-(2-pyridyl)-
carboxamide; 1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-thiazolyl)-carboxamide; 1-methyl-7-oxo-1H,7H-
pyrazolo[1,5-a]**pyrimidine**
-6-N-(2-benzothiazolyl)-carboxamide; 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[
1,5-a]**pyrimidine**-6-N-(2-thiazolyl)-
carboxamide; 1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5
-a]**pyrimidine**-6-N-(2-benzothiazolyl)-carboxamide;
1-methyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-piperidino-ethyl)-carboxamide;
1,5-dimethyl-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide; 1-(4-pyridyl)-7-oxo-
1H,7H-pyrazolo[1,5-a]**pyrimidine**
-6-N-(2-pyridyl)-carboxamide; 1-methyl-7-oxo-1H,7H-pyrazolo[1,
5-a]**pyrimidine**-6-N-(5-chloro-2-pyridyl)-carboxamide;
5-methyl-1-(2-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5-a]
pyrimidine-6-N-(2-pyridyl)-carboxamide; 1-phenyl-7-oxo-1H,7H-
pyrazolo[1,5-a]**pyrimidine**-6-carboxylic
acid; 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[1,5-a]

pyrimidine-6-carboxylic acid; 1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[1,5a]pyrimidine-6-carboxylic acid; and 5-methyl-1-(3-pyridyl)-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-carboxylic acid; or the pharmaceutically acceptable salts thereof.

6. The compound 5-methyl-1-phenyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, or the pharmaceutically acceptable salts thereof.

7. The compound 1-methyl-7-oxo-1H,7H-pyrazolo[**1,5**-a]**pyrimidine**-6-N-(2-pyridyl)-carboxamide, or the pharmaceutically acceptable salts thereof.

```
=> s deoxyuridine/cn
L11           1 DEOXYURIDINE/CN

=> d l11

L11  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   951-78-0  REGISTRY
CN   Uridine, 2'-deoxy- (6CI, 8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   1-(2-Deoxy-.beta.-D-erythro-pentofuranosyl)uracil
CN   2'-Deoxyuridine
CN   2'-Desoxyuridine
CN   2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-.beta.-D-erythro-pentofuranosyl)-
CN   2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-.beta.-D-ribofuranosyl)-
CN   Deoxyribose uracil
CN   Deoxyuridine
CN   Uracil deoxyriboside
FS   STEREOSEARCH
DR   20649-53-0
MF   C9 H12 N2 O5
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, GMELIN*,
       IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT,
       NIOSHTIC, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.
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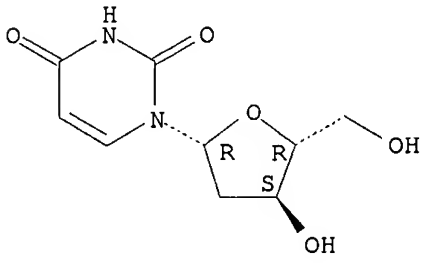


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             125 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
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                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         8.70     218.07

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HIGHEST GRANTED PATENT NUMBER: US6588018
HIGHEST APPLICATION PUBLICATION NUMBER: US2003126664
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ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 3 Jul 2003 (20030703/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
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substance identification.

=> s rheumatoid arthritis and bromovinyl and deoxyuridine
         19159 RHEUMATOID
         28485 ARTHRITIS
         17823 RHEUMATOID ARTHRITIS
                 (RHEUMATOID(W)ARTHRITIS)
           412 BROMOVINYL
          2444 DEOXYURIDINE
L12          14 RHEUMATOID ARTHRITIS AND BROMOVINYL AND DEOXYURIDINE

=> s l12 and pd<2000
       2606541 PD<2000
                 (PD<20000000)
L13           5 L12 AND PD<2000

=> d l13 1-5 bib, kwic

L13  ANSWER 1 OF 5  USPATFULL
AN     2002:34546  USPATFULL
```

TI Unique associated Kaposi's sarcoma virus sequences and uses thereof
IN Chang, Yuan, Irvington, NY, United States
Bohenzky, Roy A., Mountain View, CA, United States
Russo, James J., New York, NY, United States
Edelman, Isidore S., New York, NY, United States
Moore, Patrick S., Irvington, NY, United States
PA The Trustees of Columbia University in the City of New York, New York, NY, United States (U.S. corporation)
PI US 6348586 B1 20020219
WO 9804576 19980205 <--
AI US 1999-230371 19991117 (9)
WO 1997-US13346 19970722
19991117 PCT 371 date
RLI Continuation-in-part of Ser. No. US 1996-757669, filed on 29 Nov 1996, now patented, Pat. No. US 6183751 Continuation-in-part of Ser. No. US 1996-748640, filed on 13 Nov 1996, now patented, Pat. No. US 5854398 Continuation-in-part of Ser. No. US 1996-747887, filed on 13 Nov 1996, now patented, Pat. No. US 5853734 Continuation-in-part of Ser. No. US 1996-728323, filed on 10 Oct 1996, now patented, Pat. No. US 5948676 Continuation-in-part of Ser. No. US 1996-708678, filed on 5 Sep 1996, now patented, Pat. No. US 5859225 Continuation-in-part of Ser. No. US 1996-729615, filed on 25 Jul 1996, now abandoned Continuation-in-part of Ser. No. US 1996-687253, filed on 25 Jul 1996, now patented, Pat. No. US 5854418 Continuation-in-part of Ser. No. US 1996-686350, filed on 25 Jul 1996, now patented, Pat. No. US 5831064 Continuation-in-part of Ser. No. US 1996-686349, filed on 25 Jul 1996, now patented, Pat. No. US 5861500 Continuation-in-part of Ser. No. US 1996-686243, filed on 25 Jul 1996, now patented, Pat. No. US 5863787
DT Utility
FS GRANTED
EXNAM Primary Examiner: Bui, Phuong T.
LREP White, John P., Cooper & Durham LLP
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 29 Drawing Figure(s); 15 Drawing Page(s)
LN.CNT 6859
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 6348586 B1 20020219
WO 9804576 19980205 <--
DETD . . . is useful in treatment of an autoimmune disorder. In the most preferred embodiment, the drug is useful in treatment of **rheumatoid arthritis**.
DETD . . . is useful in treatment of an autoimmune disorder. In the most preferred embodiment, the drug is useful in treatment of **rheumatoid arthritis**.
DETD . . . is useful in treatment of an autoimmune disorder. In the most preferred embodiment, the drug is useful in treatment of **rheumatoid arthritis**.
DETD . . . Pat. No. 5,137,724 (Balzari et al. (1990) Mol. Pharm. 37,402-7) describes the use of thymidylate synthase inhibitors (e.g., 5-fluoro-uracil and 5-fluro-2'-**deoxyuridine**) in combination with compounds having viral thymidine kinase inhibiting activity.
DETD . . . its cyclic form (cHPMPC); HPMPA [(S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine] and its cyclic form (cHPMPA); (S)-HPMPDAP [(S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)-2,6-diaminopurine]; PMEDAP [9-(2-phosphonyl-methoxyethyl)-2,6-diaminopurine]; HOE 602 [2-amino-9-(1,3-bis(isopropoxy)-2-propoxymethyl)purine]; PMEA [9-(2-phosphonylmethoxyethyl)adenine]; **bromovinyl-deoxyuridine** (Burns and Sandford, 1990, J. Infect. Dis. 162:634-7); 1-.beta.-D-arabinofuranosyl-E-5-(2-**bromovinyl**)-uridine or -2'-**deoxyuridine**; BVaraU (1-.beta.-D-arabinofuranosyl-E-5-(2-**bromovinyl**)-uracil,

brovavir, Bristol-Myers Squibb, Yamsa Shoyu); BVDU [(E)-5-(2-**bromovinyl**)-2'-**deoxyuridine**, brivudin, e.g., Helpin] and its carbocyclic analogue (in which the sugar moiety is replaced by a cyclopentane ring); IVDU [(E) -5-(2-iodovinyl)-2'-**deoxyuridine**] and its carbocyclic analogue, C-IVDU (Balzarini et al., supra); and 5-mercutithio analogs of 2'-**deoxyuridine** (Holliday and Williams, 1992, Antimicrob. Agents Chemother. 36, 1935); acyclovir [9-([2-hydroxyethoxy]methyl)guanine; e.g., Zovirax (Burroughs Wellcome)]; penciclovir (9-[4-hydroxy-2-(hydroxymethyl)butyl]-guanine); ganciclovir 1(9-[1,3-dihydroxy-2 propoxymethyl]-guanine). . .

DETD Other useful antiviral agents include: 5-thien-2-yl-2A-**deoxyuridine** derivatives, e.g., BTDU [5-5(5-bromothien-2-yl)-2'-**deoxyuridine**] and CTDU [b-(5-chlorothien-2-yl)-2'-**deoxyuridine**]; and OXT-A [9-(2-deoxy-2-hydroxymethyl-.beta.-D-erythro-oxetanosyl)adenine] and OXT-G [9-(2-deoxy-2-hydroxymethyl-.beta.-D-erythro-oxetanosyl)guanine]. Although OXT-G is believed to act by inhibiting viral DNA synthesis its mechanism of. . .

DETD Certain thymidine analogs [e.g., idoxuridine (5-ido-2'-**deoxyuridine**)] and triflurothymidine) have antiherpes viral activity, but due to their systemic toxicity, are largely used for topical herpesviral infections, including. . .

DETD Brivudin is an example of an antiviral **deoxyuridine** derivative of the type described in U.S. Pat. No. 4,424,211.

DETD Brovavir is an example of an antiviral **deoxyuridine** derivative of the type described in U.S. Pat. Nos. 4,542,210 and 4,386,076.

DETD . . . mechanism of action, analytical methodology, and clinical efficacy, Therapeutic Drug Monitoring 15, 521-526; (f) Eggott et al., 1993, Antifolates in **rheumatoid arthritis**: a hypothetical mechanism of action, Clinical & Experimental Rheumatology 11 Suppl 8, S101-S105; (g) Huennekens et al., 1992, Membrane transport. . .

L13 ANSWER 2 OF 5 USPATFULL

AN 2001:121481 USPATFULL

TI Uracil reductase inactivators

IN Spector, Thomas, Durham, NC, United States
Porter, David J. T., Raleigh, NC, United States
Rahim, Saad G., Beckenham, United Kingdom

PA Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S. corporation)

PI US 6268374 B1 20010731
WO 9204901 19920402 <--

AI US 1993-30259 19930723 (8)
WO 1991-GB1650 19910925
19930723 PCT 371 date
19930723 PCT 102(e) date

DT Utility

FS GRANTED

EXNAM Primary Examiner: O'Sullivan, Peter

LREP Lemanowicz, John L.

CLMN Number of Claims: 19

ECL Exemplary Claim: 1

DRWN 2 Drawing Figure(s); 2 Drawing Page(s)

LN.CNT 817

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 6268374 B1 20010731
WO 9204901 19920402 <--

SUMM . . . and 20 minutes) by the enzyme dihydropyrimidine dehydrogenase (uracil reductase). It has been reported (Cancer Research 46, 1094, 1986) that 5-(2-**bromovinyl**)-uracil (BVU) is an inhibitor of dihydrothymidine dehydrogenase which both retards the metabolism of 5-fluorouracil and enhances its antitumour activity. It has been

reported that 5-(2-**bromovinyl**)-2'-**deoxyuridine** (which is metabolised in vivo to BVU) enhances the antitumour activity of 5-fluorouracil and 5-deoxy-5-fluorouridine, a prodrug of 5-fluorouracil (Biochemical. . .

DETD . . . useful for rescue from 5-fluorouracil toxicity; and together with 5-fluorouracil or a prodrug thereof for the treatment of psoriasis or **rheumatoid arthritis**, or human papilloma virus infections.

DETD Prodrugs of 5-fluorouracil (5-FU) are compounds which are metabolised in vivo to 5-fluorouracil and include 5-fluorouridine, 5-fluoro-2-**deoxyuridine**, 5-fluoro-2-deoxycytidine, 5'-deoxy-4',5-fluorouridine, 5'-deoxy-5-fluorouridine, 1-(2-tetrahydrofuranyl)-5-fluorouracil and 1-C.sub.1-8 alkylcarbamoyl-5-fluorouracil derivatives.

DETD . . . Chem. 19(3) 463-4 (1982) for the preparation of 5-ethynyluracil; J.Chem. Soc. Perkin Trans. 1(16), 1665-70 (1981) for the preparation of 5-(2-**bromovinyl**)uracil, 5-bromoethynyluracil and 5-(2-bromo-1-chlorovinyl)uracil; Nucleic Acid Chemistry, Vol. 2, 927-30 (1978) for the preparation 5-cyano-uracil; Nucleic Acids Research, 1(1) 105-7 (1974). . .

L13 ANSWER 3 OF 5 USPATFULL

AN 1998:157173 USPATFULL

TI Polypeptides from Kaposi's sarcoma-associated herpesvirus, DNA encoding same and uses thereof

IN Chang, Yuan, New York, NY, United States
Bohenzky, Roy A., Mountian View, CA, United States
Russo, James J., New York, NY, United States
Edelman, Isidore S., New York, NY, United States
Moore, Patrick S., New York, NY, United States

PA The Trustees of Columbia University in the City of New York, New York, NY, United States (U.S. corporation)

PI US 5849564 19981215 <--

AI US 1996-770379 19961129 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Myers, Carla J.

LREP White, John P.Cooper & Dunham LLP

CLMN Number of Claims: 12

ECL Exemplary Claim: 1,6,7

DRWN 29 Drawing Figure(s); 16 Drawing Page(s)

LN.CNT 6146

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5849564 19981215 <--

DETD . . . is useful in treatment of an autoimmune disorder. In the most preferred embodiment, the drug is useful in treatment of **rheumatoid arthritis**.

DETD . . . is useful in treatment of an autoimmune disorder. In the most preferred embodiment, the drug is useful in treatment of **rheumatoid arthritis**.

DETD . . . is useful in treatment of an autoimmune disorder. In the most preferred embodiment, the drug is useful in treatment of **rheumatoid arthritis**.

DETD . . . Pat. No. 5,137,724 (Balzari et al. (1990) Mol. Pharm. 37,402-7) describes the use of thymidylate synthase inhibitors (e.g., 5-fluoro-uracil and 5-fluro-2'-**deoxyuridine**) in combination with compounds having viral thymidine kinase inhibiting activity.

DETD . . . (cHPMPA); (S)-HPMPDAP [(S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)-2,6-diaminopurine]; PMEDAP [9-(2-phosphonyl-methoxyethyl)-2,6-diaminopurine]; HOE 602 [2-amino-9-(1,3-bis (isopropoxy)-2-propoxymethyl)purine]; PMEA [9-(2-phosphonylmethoxyethyl)adenine]; bromovinyldeoxyuridine (Burns and Sandford, 1990, J. Infect. Dis. 162:634-7); 1-.beta.-D-arabinofuranosyl-

E-5-(2-**bromovinyl**)-uridine or -2'-**deoxyuridine**; BVaraU (1-.beta.-D-arabinofuranosyl-E-5-(2-**bromovinyl**)-uracil, brovavir, Bristol-Myers Squibb, Yamsa Shoyu); BVDU [(E)-5-(2-**bromovinyl**)-2'-**deoxyuridine**, brivudin, e.g., Helpin] and its carbocyclic analogue (in which the sugar moiety is replaced by a cyclopentane ring); IVDU [(E)-5-(2-iodovinyl)-2'-**deoxyuridine**] and its carbocyclic analogue, C-IVDU (Balzarini et al., supra); and 5-mercutithio analogs of 2'-**deoxyuridine** (Holliday and Williams, 1992, Antimicrob. Agents Chemother. 36, 1935); acyclovir [9-([2-hydroxyethoxy]methyl)guanine; e.g., Zovirax (Burroughs Wellcome)]; penciclovir (9-[4-hydroxy-2-(hydroxymethyl)butyl]-guanine); ganciclovir [(9-[1,3-dihydroxy-2 propoxymethyl]-guanine). . .

DETD Other useful antiviral agents include: 5-thien-2-yl-2'-**deoxyuridine** derivatives, e.g., BTDU [5-5(5-bromothien-2-yl)-2'-**deoxyuridine**] and CTDU [b-(5-chlorothien-2-yl) -2'-**deoxyuridine**]; and OXT-A [9-(2-deoxy-2-hydroxymethyl-.beta.-D-erythro-oxetanosyl)adenine] and OXT-G [9-(2-deoxy-2-hydroxymethyl-.beta.-D-erythrooxetanosyl)guanine]. Although OXT-G is believed to act by inhibiting viral DNA synthesis its mechanism of. . .

DETD Certain thymidine analogs [e.g., idoxuridine (5-ido-2'-**deoxyuridine**)] and triflurothymidine) have antiherpes viral activity, but due to their systemic toxicity, are largely used for topical herpesviral infections, including. . .

DETD Brivudin is an example of an antiviral **deoxyuridine** derivative of the type described in U.S. Pat. No. 4,424,211.

DETD Brovavir is an example of an antiviral **deoxyuridine** derivative of the type described in U.S. Pat. Nos. 4,542,210 and 4,386,076.

DETD . . . mechanism of action, analytical methodology, and clinical efficacy, Therapeutic Drug Monitoring 15, 521-526; (f) Eggott et al., 1993, Antifolates in **rheumatoid arthritis**: a hypothetical mechanism of action, Clinical & Experimental Rheumatology 11 Suppl 8, S101-S105; (g) Huennekens et al., 1992, Membrane transport. . .

L13 ANSWER 4 OF 5 USPATFULL

AN 1998:150919 USPATFULL

TI 5-Fluorouracil derivatives

IN Boyd, Frank Leslie, Raleigh, NC, United States
Krenitsky, Thomas Anthony, Chapel Hill, NC, United States

PA Glaxo Wellcome Inc., Five Moore Drive, NC, United States (U.S. corporation)

PI US 5843917 19981201 <--
WO 9512606 19950511 <--

AI US 1996-612911 19960502 (8)
WO 1994-GB2428 19941104
19960502 PCT 371 date
19960502 PCT 102(e) date

PRAI GB 1993-22795 19931105

DT Utility

FS Granted

EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Qazi, Sabiha N.

LREP Hrubiec, Robert T.

CLMN Number of Claims: 3

ECL Exemplary Claim: 1

DRWN 1 Drawing Figure(s); 1 Drawing Page(s)

LN.CNT 1089

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5843917 19981201 <--
WO 9512606 19950511 <--

SUMM . . . and 20 minutes) by the enzyme dihydrothymidine dehydrogenase (uracil reductase). It has been reported (Cancer Research 46, 1094, 1986) that 5-(2-**bromovinyl**)-uracil (BVU) is an inhibitor of

dihydrothymidine dehydrogenase which both retards the metabolism of 5-fluorouracil and enhances its antitumour activity. It has been reported that 5-(2-**bromovinyl**)-2'-**deoxyuridine** (which is metabolised in vivo to BVU) enhances the antitumour activity of 5-fluorouracil and 5-deoxy-5-fluorouridine, a prodrug of 5-fluorouracil (Biochemical. . .

SUMM Prodrugs of 5-fluorouracil are compounds which are metabolised in vivo to 5-fluorouracil and include 5-fluorouridine, 5-fluoro-2-**deoxyuridine**, 5-fluoro-2-deoxycytidine, 5'-deoxy-5-fluorouridine, 1-(2-tetrahydrofuranyl)-5-fluorouracil and 1-C.sub.1-8 alkylcarbamoyl-5-fluorouracil derivatives.

SUMM . . . manufacture of a medicament for use in cancer chemotherapy. The medicament may also be useful for the treatment of psoriasis, **rheumatoid arthritis**, or human papilloma virus infections.

SUMM a) A method for the treatment or prophylaxis of psoriasis, **rheumatoid arthritis** or human papilloma virus infection which comprises administering an effective amount of a compound as hereinbefore defined to a mammal;

DETD (a) 5'-O-(tert-Butyldimethylsilyl)-2'-deoxy-5-fluorouridine 5-Fluoro-2'-**deoxyuridine** (United States Biochemical Corporation, Cleveland, Ohio 44120) (6.00 g, 24.4 mmol) and 3.65 g (5.36 mmol) imidazole (Aldrich Chemical Company,. . .

DETD 5-Iodo-2'-**deoxyuridine** (United States Biochemical Corporation, Cleveland Ohio 44120) (10.0 g, 28.2 mmol) and 4.23 g (62.1 mmol) of imidazole (Aldrich Chemical. . .

DETD 5-Fluoro-2'-**deoxyuridine** (United States Biochemical Corporation, Cleveland, Ohio 44120) (1.0 g, 4.1 mmol) was twice suspended in 30 ml anhydrous pyridine in. . .

DETD (b) 2'-Deoxy-5-iodo-5'-O-(4-Methoxytrityl)uridine 5-Iodo-2'-**deoxyuridine** (United States Biochemical Corporation, Cleveland, Ohio 44120) (1.0 g, 2.8 mmol) was twice suspended in 30 ml anhydrous pyridine in. . .

DETD A mixture of 5-iodo-2'-**deoxyuridine** (U.S. Biochemical Corp., Cleveland, Ohio) (2.7 mmol), dimethylformamide (8 ml), and triethylamine (0.6 ml) was deoxygenated with a rapid stream. . .

L13 ANSWER 5 OF 5 USPATFULL
AN 1998:122415 USPATFULL
TI Uracil reductase inactivators
IN Spector, Thomas, Durham, NC, United States
Porter, David J. T., Raleigh, NC, United States
Rahim, Saad G., Beckenham, United Kingdom
PA Glaxo Wellcome Inc., RTP, NC, United States (U.S. corporation)
PI US 5817664 19981006 <--
AI US 1995-470317 19950606 (8)
RLI Division of Ser. No. US 1993-30259, filed on 23 Jul 1993
PRAI GB 1990-20930 19900926
DT Utility
FS Granted
EXNAM Primary Examiner: O'Sullivan, Peter
LREP Hrubiec, Robert T.
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 836
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5817664 19981006 <--

SUMM . . . and 20 minutes) by the enzyme dihydropyrimidine dehydrogenase (uracil reductase). It has been reported (Cancer Research 46, 1094, 1986) that 5-(2-**bromovinyl**)-uracil (BVU) is an inhibitor of dihydrothymidine dehydrogenase which both retards the metabolism of

5-fluorouracil and enhances its antitumour activity. It has been reported that 5-(2-**bromovinyl**)-2'-**deoxyuridine** (which is metabolised in vivo to BVU) enhances the antitumour activity of 5-fluorouracil and 5-deoxy-5-fluorouridine, a prodrug of 5-fluorouracil (Biochemical. . .

SUMM . . . useful for rescue from 5-fluorouracil toxicity; and together with 5-fluorouracil or a prodrug thereof for the treatment of psoriasis or **rheumatoid arthritis**, or human papilloma virus infections.

SUMM . . . reference to prodrugs thereof. Prodrugs of 5-fluorouracil (5-FU) are compounds which are metabolised in vivo to 5-fluorouracil and include 5-fluorouridine, 5-fluoro-2-**deoxyuridine**, 5-fluoro-2-deoxycytidine, 5'-deoxy-4',5-fluorouridine, 5'-deoxy-5-fluorouridine, 1-(2-tetrahydrofuranyl)-5-fluorouracil and 1-C.sub.1-8 alkylcarbamoyl-5-fluorouracil derivatives. 5-FU or a prodrug thereof and the said 5-uracil derivative may be. . .

SUMM . . . Chem. 19(3) 46-4 (1982) for the preparation of 5-ethynyluracil: J.Chem. Soc. Perkin Trans. 1(16), 1665-70 (1981) for the preparation of 5-(2-**bromovinyl**)uracil, 5-bromoethynyluracil and 5-(2-bromo-1-chlorovinyl)uracil: Nucleic Acid Chemistry, Vol. 2, 927-30 (1978) for the preparation 5-cyano-uracil; Nucleic Acids Research, 1(1) 105-7 (1974). . .

```
=> s phosphoryl/cn
L15             1 PHOSPHORYL/CN

=> d l15

L15  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   14452-66-5  REGISTRY
CN   Phosphorus oxide (PO) (6CI, 7CI, 8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Phosphorus monoxide
CN   Phosphoryl
CN   Phosphoryl radical
DR   12169-19-6
MF   O P
CI   COM
LC   STN Files:   BIOSIS, CA, CAOLD, CAPLUS, DETHERM*, GMELIN*, NIOSHTIC,
       TOXCENTER, USPATFULL
         (*File contains numerically searchable property data)


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               2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             292 REFERENCES IN FILE CAPLUS (1957 TO DATE)
              31 REFERENCES IN FILE CAOLD (PRIOR TO 1967)
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FULL ESTIMATED COST	48.98	49.19

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FULL ESTIMATED COST	48.98	49.19

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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 3 Jul 2003 (20030703/PD)
FILE LAST UPDATED: 3 Jul 2003 (20030703/ED)
HIGHEST GRANTED PATENT NUMBER: US6588018
HIGHEST APPLICATION PUBLICATION NUMBER: US2003126664
CA INDEXING IS CURRENT THROUGH 3 Jul 2003 (20030703/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 3 Jul 2003 (20030703/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
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>>>  classifications, or claims, that may potentially change from      <<<
>>>  the earliest to the latest publication.                           <<<

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substance identification.

=> s furan? and pyrimidone
         34013 FURAN?
           788 PYRIMIDONE
L3         227 FURAN? AND PYRIMIDONE

=> s l3 and rheumatoid arthritis
         19159 RHEUMATOID
         28485 ARTHRITIS
         17823 RHEUMATOID ARTHRITIS
                 (RHEUMATOID(W)ARTHRITIS)
L4          42 L3 AND RHEUMATOID ARTHRITIS

=> s l4 and pd<2000
       2606541 PD<2000
                 (PD<20000000)
L5          13 L4 AND PD<2000

=> d l5 1-13 bib, ab, kwic

L5   ANSWER 1 OF 13  USPATFULL
AN     2002:168227  USPATFULL
TI     Pyrimidinone compounds and pharmaceutical compositions containing them
IN     Hickey, Deirdre Mary Bernadette, Saffron Walden, UNITED KINGDOM
       Ife, Robert John, Stevenage, UNITED KINGDOM
       Leach, Colin Andrew, Stevenage, UNITED KINGDOM
       Pinto, Ivan Leo, Sutton, UNITED KINGDOM
       Porter, Roderick Alan, Bishops Stortford, UNITED KINGDOM
       Smith, Stephen Allan, Bishops Stortford, UNITED KINGDOM
PA     SmithKline Beecham p.l.c., UNITED KINGDOM (non-U.S. corporation)
PI     US 6417192          B1   20020709
       WO 9924420  19990520                                          <--
AI     US 2000-530713           20000628 (9)
       WO 1998-EP6988           19981023
                                20000628  PCT 371 date
PRAI   GB 1997-23352       19971106
       GB 1997-23358       19971106
DT     Utility
FS     GRANTED
EXNAM  Primary Examiner: Raymond, Richard L.; Assistant Examiner: McKenzie,
       Thomas C
LREP   Kanagy, James M., Kinzig, Charles M.
CLMN   Number of Claims: 17
ECL    Exemplary Claim: 1
DRWN   0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 6447
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     A group of novel pyrimidone compounds are inhibitors of the
       enzyme LDL PLA.sub.2 and therefore of use in treating atherosclerosis.
PI     US 6417192          B1   20020709
       WO 9924420  19990520                                          <--
AB     A group of novel pyrimidone compounds are inhibitors of the
       enzyme LDL PLA.sub.2 and therefore of use in treating atherosclerosis.
SUMM   . . . recombinant host cells transformed with DNA encoding the
       enzyme. Suggested therapeutic uses for inhibitors of the enzyme included
       atherosclerosis, diabetes, rheumatoid arthritis,
       stroke, myocardial infarction, reperfusion injury and acute and chronic
```

inflammation. A subsequent publication from the same group further describes this. . .

SUMM . . . to produce the two injurious products, lysophosphatidylcholine and oxidatively modified fatty acids. Such conditions include the aforementioned conditions atherosclerosis, diabetes, **rheumatoid arthritis**, stroke, myocardial infarction, reperfusion injury and acute and chronic inflammation. Further such conditions include various neuropsychiatric disorders such as schizophrenia. . .

SUMM . . . (Tew et al, Biochemistry, 37, 10087, 1998). GB 1 582 527 describes, as compounds of formula (7), a group of **pyrimidone** compounds of the formula (A): ##STR1##

SUMM A new class of **pyrimidone** compounds has now been identified which are inhibitors of the enzyme Lp-PLA.sub.2.

SUMM . . . when an aryl group include phenyl and naphthyl. Representative examples of R.sup.2 when a heteroaryl group include pyridyl, pyrimidinyl, pyrazolyl, **furanyl**, thienyl, thiazolyl, quinolyl,benzothiazolyl, pyridazolyl and pyrazinyl Preferably, R.sup.2 is phenyl optionally substituted by 1, 2 or 3 substituents selected from. . .

SUMM . . . substituents include aryl, preferably phenyl which may be optionally substituted by COOC.sub.(1-6)alkyl (e.g methyl) and heteroaryl (for instance pyridyl, imidazolyl, **furanyl**, thienyl and 2-oxo pyrrolidinyl). Preferred examples of the substituent NR.sup.11R.sup.12 include morpholino, piperidino or 2-oxo-pyrrolidino group.

SUMM . . . monocyclic with 5 to 6 members and one or two heteroatoms selected from nitrogen, oxygen and sulphur, such as pyridyl, **furanyl**, thienyl and imidazolyl. A further preferred subgroup of compounds of formula (I) are those in which W is a bond. . .

SUMM . . . in conjunction with enzyme activity, for example in addition to conditions such as atherosclerosis and diabetes, other conditions such as **rheumatoid arthritis**, stroke, inflammatory conditions of the brain such as Alzheimer's Disease, myocardial infarction, reperfusion injury, sepsis, and acute and chronic inflammation.. . .

DETD The appropriate 2-(nitroamino)**pyrimidone** (1 equiv) and thiol (2 equiv) in pyridine (ca 2 ml per mmol) were stirred at reflux for 2 days,. . .

DETD C3. Similar to method C2, except that the solvent was 1,2-dichloroethane in place of dichloromethane, and the **pyrimidone** was treated with tributyltin chloride (1 equiv) and stirred overnight to form the silyl ether before addition of the alkylating. . .

DETD 1-(**Furan**-2-ylmethyl)-2-(3,4-difluorobenzyl)thio-5-(2-methoxypyrimid-5-ylmethyl)pyrimidin-4-one

L5 ANSWER 2 OF 13 USPATFULL

AN 2001:97935 USPATFULL

TI Hydroxamic acids substituted by heterocycles useful for inhibition of tumor necrosis factor

IN Bird, Thomas Geoffrey Colerick, Reims, France

PA Zeneca Limited, London, United Kingdom (non-U.S. corporation)
Zeneca Pharma S.A., Cergy Cedex, France (non-U.S. corporation)

PI US 6251913 B1 20010626
WO 9843959 19981008 <--

AI US 1999-381836 19990924 (9)
WO 1998-GB910 19980325
19990924 PCT 371 date
19990924 PCT 102(e) date

PRAI EP 1997-400725 19970328

DT Utility

FS GRANTED

EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner:

Balasubramanian, Venkataraman
LREP Pillsbury Winthrop LLP
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1631
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of formula (I), ##STR1##

wherein: n is 1 to 6; Het is a nitrogen containing ring fused to the benzene ring on two adjacent carbon atoms to form a bicyclic ring system which ring system may be optionally substituted; R.sup.1 is hydrogen, C.sub.1-8 alkyl, C.sub.2-6 alkenyl, C.sub.2-6 alkyny, C.sub.3-8 cycloalkyl, aryl, heteroaryl, heterocyclyl, arylC.sub.1-6 alkyl, heteroarylC.sub.1-6 alkyl, heterocyclylC.sub.1-6 alkyl or C.sub.3-8 cycloalkylC.sub.1-6 alkyl; R.sup.2 is C.sub.1-6 alkyl, C.sub.2-6 alkenyl, arylC.sub.1-6 alkyl, heteroarylC.sub.1-6 alkyl or the side-chain of a naturally occurring amino acid; R.sup.3 is hydrogen, C.sub.1-6 alkyl, C.sub.3-8 cycloalkyl, C.sub.4-8 cycloalkenyl, arylC.sub.1-6 alkyl, heteroarylC.sub.1-6 alkyl or heterocycylC.sub.1-6 alkyl; R.sup.4 is hydrogen or C.sub.1-6 alkyl; or R.sup.3 and R.sup.4 together with the nitrogen atom to which they are joined form a heterocyclic ring; wherein any group or ring, in R.sup.1 -R.sup.4, is optionally substituted; and pharmaceutically acceptable salts and in vivo hydrolysable esters thereof, are described as inhibitors of the production of Tumor Necrosis Factor and/or one or more matrix metalloproteinase enzymes. Compositions containing them and their preparation are also described.

PI US 6251913 B1 20010626
WO 9843959 19981008 <--

SUMM . . . implicated in mediating or exacerbating the development of various inflammatory and allergic diseases such as inflammation of the joints (especially **rheumatoid arthritis**, osteoarthritis and gout), inflammation of the gastrointestinal tract inflammatory bowel disease, ulcerative colitis and gastritis), skin disease (especially psoriasis, eczema. . .

SUMM . . . ring with up to five ring heteroatoms selected from nitrogen, oxygen and sulphur. Examples of `heteroaryl ` include thienyl, pyrrolyl, **furanyl**, imidazolyl, thiazolyl, pyrimidinyl, pyridinyl, indolyl, benzimidazolyl, benzthiazolyl, quinolinyl and isoquinolinyl. "Heterocyclyl" in the terms "heterocyclyl" and heterocyclyl-C.sub.1-6 alkyl" means a. . .

SUMM In another aspect Het is a pyridone or **pyrimidone** ring such as of the sub-formulae (i)-(iii): ##STR3##

SUMM Preferably Het is a pyridone or **pyrimidone** ring of the sub-formula (ii) or (iii).

L5 ANSWER 3 OF 13 USPATFULL
AN 1999:155727 USPATFULL
TI Pyrrolopyrrolone derivatives as inhibitors of neutrophil elastase
IN Dowle, Michael Dennis, Ware, United Kingdom
Finch, Harry, Letchworth, United Kingdom
Harrison, Lee Andrew, Biggleswade, United Kingdom
Inglis, Graham George, Kingswood, United Kingdom
Johnson, Martin Redpath, Royston, United Kingdom
Macdonald, Simon John Fawcett, Benington, United Kingdom
Shah, Pritom, Biggleswade, United Kingdom
Smith, Robin Andrew, St. Albans, United Kingdom
PA Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S. corporation)
PI US 5994344 19991130 <--
WO 9736903 19971009 <--

AI US 1998-155323 19980925 (9)
WO 1997-EP1530 19970326
19980925 PCT 371 date
19980925 PCT 102(e) date
PRAI GB 1996-6508 19960328
GB 1996-23001 19961105
DT Utility
FS Granted
EXNAM Primary Examiner: Stockton, Laura L.
LREP Riek, James P.
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6230
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There are described according to the invention compounds of formula (I) (relative stereochemistry indicated), wherein R.sub.1, R.sub.2, R.sub.3 and X are as defined in the specification, together with processes for preparing them, compositions containing them and their use as pharmaceuticals. Compounds of formula (I) are indicated inter alia for the treatment of chronic bronchitis.
PI US 5994344 19991130 <--
WO 9736903 19971009 <--
SUMM . . . heteroatoms. Suitable R.sub.1 heteroaryl groups will have up to two rings. Examples include imidazolyl, optionally N-substituted by C.sub.1-4 alkyl; pyridyl; **furanyl**; pyrrolyl and thienyl.
SUMM Preferred R.sub.1 groups include C.sub.2-8 alkenyl-NR.sub.4 R.sub.5 ; phenyl, **furanyl**, thiophenyl or pyrrolyl substituted by the group (CH.sub.2).sub.n' --NR.sub.4 R.sub.5 (wherein n' represents an integer 1 to 5) and phenyl. . .
SUMM Compounds of the invention may also be useful in the treatment of connective issue disorders such as **rheumatoid arthritis**, osteoarthritis and spondylitis and inflammatory conditions of the kidney such as glomerulonephritis.
DETD . . . 40 ml) was added dropwise to a stirred solution of Intermediate 63 (16.13 g) in a dry tetrahydrofuran (86 ml) 1:3-dimethyl-3,4,5,6-tetrahydro-2H-(1H)-**pyrimidone** (200 ml) mixture at -51.degree. C. under nitrogen. The mixture was then cooled to -64.degree. C. and more LHMDS in. . .
DETD rel-5-(6R-Isopropyl-4-methanesulfonyl-5-oxo-hexahydro-(3aS,6aR)-pyrrolo[3,2-b]pyrrole-1-carbonyl)-**furan**-2-carbaldehyde
DETD rel-(3R,3aR,6aS)-4-(**Furan**-2-carbonyl)-1-methanesulfonyl-3-propyl-hexahydropyrro!o[3,2-b]pyrrol-2-one
DETD rel-(3R,3aR,6aS)-4-(**Furan**-2-carbonyl)-3-isopropyl-1-methanesulfonyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one
DETD rel-(3R,3aR,6aS)-3-Isopropyl-1-methanesulfonyl-4-(5-piperidin-1-ylmethyl-**furan**-2-carbonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one hydrochloride
DETD rel-(3R,3aR-6aS)-4-(5-Dimnethylaminomethyl-**furan**-2-carbonyl)-3-isopropyl-1-methanesulfonyl-hexahydro-pyrrolo[T3,2-b]pyrrol-2-one hydrochloride
DETD rel-(3R,3aR,6aS)-4-(5-Cycloproptl minomethtli-**furan**-2-carbonyl)-3-isopropyl-1-methanesulfonyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one hydrochloride
CLM What is claimed is:
10. A compound according to claim 1, wherein R.sub.1 represents phenyl, **furanyl**, thiophenyl or pyrrolyl substituted by the group -(CH.sub.2).sub.m --NR.sub.4 R.sub.5 and m represents an integer 1 to 5.

. . . 2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-4-[4-(2-oxo-pyrrolidin-1-yl)-benzenesulfonyl]-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-N-[2-Chloro4-(4-methanesulfonyl-5-oxo-6R-propyl-hexahydro-(3aS,6aR)-

pyrrolo[3,2-b]pyrrole-1-sulfonyl)-phenyl]-acetamide; rel-(3R,3aR,6aS)-4-(4-Butoxy-benzenesulfonyl)-1-methanesulfonyl-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(4-Chloro-benzenesulfonyl)-1methanesulfonyl-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-3-propyl4-(4-trifluoromethyl-benzenesulfonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-4-(4-methanesulfonyl-benzenesulfonyl)-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-4-(4-Methanesulfonyl-5-oxo-6R-propyl-hexahydro-(3aS,6aR)-pyrrolo[3,2b]pyrrole-1-sulfonyl)-benzonitrile; rel-(3R,3aR,6aS)-4-Benzenesulfonyl-1-methanesulfonyl-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-4-(4-methoxy-benzenesulfonyt)-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(4-Dimethylamino-benzenesulfonyl)-1-methanesulfonyl-3-propyl-hexahydropyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-4-(3-nitro-benzenesulfonyl)-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-3-propyl4-(3-trifluoromethyl-benzenesulfonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(3,5-Bis-trifluoromethyl-benzenesulfonyl)-1-methanesulfonyl-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-3-propyl4-(2-trifluoromethyl-benzenesuffonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-4-(2-nitro-benzenesulfonyl)-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-3-Isopropyl-1-methanesulfonyl-4-(4-methanesulfonyl-benzenesulfonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-3-Isopropyl-1-methanesuffonyl-4-(4-trifluoromethyl-benzenesulfonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-3-Isopropyl-1-methanesulfonyl-4-(4-nitro-benzenesulfonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(4-Butoxy-benzenesulfonyl)-3-isopropyl-1-methanesulfonyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(**Furan**-2-carbonyl)-1-methanesulfonyl-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-3-propyl-4-(thiophene-2-carbonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-Benzoyl-1-methanesulfonyl-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(4-Amino-benzenesulfonyl)-1-methanesulfonyl-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(3-Amino-benzenesulfonyl)-1-methanesulfonyl-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(2-Amino-benzenesulfonyl)-1-methanesulfonyl-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(4-Amino-benzenesulfonyl)-3-isopropyl-1-methanesulfonyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-3-propyl-4-(pyridine-2-carbonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(4-Butoxy-benzoyl)-1-methanesulfonyl-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-4-(1-methyl-1H-pyrrol2-carbonyl)-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-N-[15-(4-Methanesulfonyl-5-oxo-6R-propyl-hexahydro-(3aS,6aR)-pyrrolo[3,2-b]pyrrole-1-carbonyl)-pyridin-2-yl]-acetamide; rel-(3R,3aR,6aS)-1-Methanesulfonyl-3-propyl-4-(1H-pyrrole-2-carbonyl-)hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-3-propyl-4-(4-trifluoromethyl-benzoyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-3-propyl-4-(4-trifluoromethyl-benzoyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-4-(4-methanesulfonyl-benzoyl)-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-3-propyl4-(pyridine4-carbonyl-)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-3-propyl4-(pyridine-3-carbonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(**Furan**-2-carbonyl)-3-isopropyl-1-methanesulfonyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-3-Isopropyl-1-methanesulfonyl-4-(thiophene-2-carbonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-

2-one; rel-(3R,3aR,6aS)-3-Isopropyl-1-methanesulfonyl-4-(5-piperidin-1-ylmethyl-**furan**-2-carbonyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(5-Dimethylaminomethyl-**furan**-2-carbonyl)-3-isopropyl-1-methanesulfonyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(5-Cyclopropylaminomethyl-**furan**-2-carbonyl)-3-isopropyl-1-methanesulfonyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-4-(3-Dimethylaminomethyl-benzoyl)-3-isopropyl-1 -methanesulfonyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-1-Methanesulfonyl-4-[4-(4-methyl-piperazin-1-yl)-but-2E-enoyl]-3-propyl-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-3-Isopropyl-1-methanesulfonyl-4-(4-piperidin-4-yl-butyryl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-3-Isopropyl-1-methanesulfonyl-4-[4-(1-methyl-piperidin-4-yl)-butyryl]-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; rel-(3R,3aR,6aS)-3-Cyclopropyl-1-methanesulfonyl-4-(4-piperidin-1-yl-but-2E-enoyl)-hexahydro-pyrrolo[3,2-b]pyrrol-2-one; or a pharmaceutical acceptable salt, solvate or enantiomer of any one thereof.

L5 ANSWER 4 OF 13 USPATFULL
AN 1998:12025 USPATFULL
TI .alpha.-(1,3-dicarbonylenol ether) methyl ketones as cysteine protease inhibitors
IN Zimmerman, Mary P., Pleasonton, CA, United States
Smith, Robert E., Livermore, CA, United States
Becker, Mark, Walnut Creek, CA, United States
PA Prototek, Inc., Dublin, CA, United States (U.S. corporation)
PI US 5714484 19980203 <--
AI US 1995-481808 19950607 (8)
RLI Continuation-in-part of Ser. No. US 1993-164031, filed on 8 Dec 1993, now patented, Pat. No. US 5486623
DT Utility
FS Granted
EXNAM Primary Examiner: Shah, Mukuno J.; Assistant Examiner: Ngo, Tamthom T.
LREP Woodard, Emhardt, Naughton, Moriarty & McNett
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1647
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Cysteine protease inhibitors which deactivate the protease by covalently bonding to the cysteine protease and releasing the enolate of a 1,3-dicarbonyl (or its enolic form). The cysteine protease inhibitors of the present invention accordingly comprise a first portion which targets a desired cysteine protease and positions the inhibitor near the thiolate anion portion of the active site of the protease, and a second portion which covalently bonds to the cysteine protease and irreversibly deactivates that protease by providing a carbonyl or carbonyl-equivalent which is attacked by the thiolate anion of the active site of the cysteine protease to sequentially cleave a .beta.-dicarbonyl enol ether leaving group.
PI US 5714484 19980203 <--
SUMM . . . substrate technology and by natural endogenous inhibitors as playing a causative role in a number of disease states such as **rheumatoid arthritis**, osteo arthritis, pneumocystis carinii, schistosomiasis, trypanosoma cruzi, trypanosoma brucei brucei, Crithidia fusiculata, malaria, periodontal disease, tumor metastasis, metachromatic leukodystrophy, muscular dystrophy, etc. For example, a connection between cathepsin B-type enzymes and **rheumatoid arthritis** has been suggested in van Noorden and Everts, "Selective Inhibition of Cysteine Proteinases by Z-Phe-Ala-CH.sub.2 F Suppresses Digestion of Collagen. . .
SUMM . . . acid wherein the heterocycle is a piperazine, a

decahydroisoquinoline, a pyrrolinone, a pyridine, a pyridone, a carbolinone, a quinazoline, a **pyrimidone** or the like;

SUMM . . . acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a pyridone, a carbolinone, a quinazoline, a **pyrimidone** or the like;

SUMM . . . acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a pyridone, a carbolinone, a quinazoline, a **pyrimidone** or the like;

SUMM . . . acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a pyridone, a carbolinone, a quinazoline, a **pyrimidone** or the like;

SUMM . . . acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a pyridone, a carbolinone, a quinazoline, a **pyrimidone** or the like;

SUMM . . . acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a pyridone, a carbolinone, a quinazoline, a **pyrimidone** or the like;

SUMM . . . acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a pyridone, a carbolinone, a quinazoline, a **pyrimidone** or the like;

DETD . . . the amino acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a carbolinone, a quinazoline, a **pyrimidone** or the like;

DETD . . . the amino acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a carbolinone, a quinazoline, a **pyrimidone** or the like;

DETD . . . the amino acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a carbolinone, a quinazoline, a **pyrimidone** or the like;

DETD . . . the amino acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a carbolinone, a quinazoline, a **pyrimidone** or the like;

DETD . . . the amino acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a carbolinone, a quinazoline, a **pyrimidone** or the like;

DETD . . . the amino acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a carbolinone, a quinazoline, a **pyrimidone** or the like;

DETD . . . the amino acid wherein the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a carbolinone, a quinazoline, a **pyrimidone** or the like;

DETD . . . a heterocyclic replacement. Preferably the heterocycle is a piperazine, a decahydroisoquinoline, a pyrrolinone, a pyridine, a carbolinone, a quinazoline, a **pyrimidone** or the like. Persons skilled in the art may select an appropriate heterocycle in a manner similar to that in. . .

DETD N-Morpholinecarbonyl-L-phenylalanyl-L-homophenylalanyl-.alpha.-(3-oxy-5-ethyl-4-methyl 2(5H) **furanone**) methyl ketone (A2). MuPheHPheCH.sub.2 Br (100 mg), potassium fluoride (45 mg), and 5-ethyl-3-hydroxy-4-methyl-2(5H) **furanone** (110 mg) was placed under argon in 5 mL of dry DMF and the reaction was stirred at room temperature. . .

DETD . . . in methylene chloride; (g) Nmethyl morpholine, isobutyl chloroformate then an unblocke amino acid alpha oxyheterocycle methyl ketone such as Lhomophenyl-alpha-4-oxy-dihdro- **furan2**-one) methyl ketone (example

9); (h
Nmethyl morpholine, isobutyl chloroformate, then diazomethane/ether from
Diazald (Aldrich); 30% HBr/acetic acid in methylene chloride;. . .

L5 ANSWER 5 OF 13 USPATFULL
AN 96:14816 USPATFULL
TI Substituted quinolyl compounds exhibiting selective leukotriene B.sub.4 antagonist activity
IN Dereu, Norbert, Viry-Chatillon, France
Hendel, Wolfram, Leonding, Austria
Labaudiniere, Richard, Vitry-sur-Seine, France
PA Rhone-Poulenc Rorer S.A., Antony Cedex, France (non-U.S. corporation)
PI US 5492915 19960220 <--
AI US 1994-318919 19941006 (8)
RLI Division of Ser. No. US 1993-966151, filed on 17 Feb 1993, now patented, Pat. No. US 5366982
PRAI FR 1990-9453 19900724
DT Utility
FS Granted
EXNAM Primary Examiner: Henley, III, Raymond; Assistant Examiner: Spivack, Phyllis G.
LREP Nicholson, James A., Savitzky, Martin F., Parker, III, Raymond S.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2961
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to compounds having selective LTB.sub.4 antagonist properties. Therapeutic compositions comprising said compounds and methods for the treatment of disorders involving LTB.sub.4 agonist-mediated activity utilizing said compositions wherein the compounds are described by the formula ##STR1## wherein R.sub.4, X, R, Y, R', Q, m and n are herein defined, and pharmaceutically acceptable salts thereof.
PI US 5492915 19960220 <--
SUMM "Monocyclic aryl" means a partially or completely unsaturated carbocyclic or heterocyclic ring. Preferred monocycles include benzene, thiophene, pyridine, **furan** and pyrimidine.
DETD 4,5-bis-(4-chlorophenyl)-2-**pyrimidone**
DETD 4,5-diphenyl-2-**pyrimidone**
DETD 4,5-bis-(4-methoxyphenyl)-2-**pyrimidone**
DETD . . . such possess therapeutic value in the treatment of Inflammatory conditions and hypersensitivity responses. LTB.sub.4 is implicated in diseases such as **rheumatoid arthritis**, gout, psoriasis and inflammatory bowel disease and therefore compounds which demonstrate LTB.sub.4 antagonist properties are useful in the control of. . .

L5 ANSWER 6 OF 13 USPATFULL
AN 94:102245 USPATFULL
TI Substituted bicyclic bis-aryl compounds exhibiting selective leukotriene B.sub.4 antagonist activity, their preparation and use in pharmaceutical compositions
IN Dereu, Norbert, Viry-Chatillon, France
Hendel, Wolfram, Leonding, Austria
Labaudiniere, Richard, Vitry-sur-Seine, France
PA Rhone-Poulenc Rorer S.A., Antony, France (non-U.S. corporation)
PI US 5366982 19941122 <--
WO 9201675 19920206 <--
AI US 1993-966151 19930217 (7)
WO 1991-EP1341 19910718
19930217 PCT 371 date

19930217 PCT 102(e) date
PRAI FR 1990-9453 19900724
DT Utility
FS Granted
EXNAM Primary Examiner: Cintins, Marianne M.; Assistant Examiner: Spivack, Phyllis G.
LREP Nicholson, James A., Savitzky, Martin F., Parker, III, Raymond S.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2950
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to compounds having selective LTB.sub.4 antagonist properties, compositions comprising said compounds and methods for the treatment of disorders involving LTB.sub.4 agonist-mediated activity utilizing said compositions wherein the compounds are described by the general formula ##STR1## and pharmaceutically acceptable salts thereof.
PI US 5366982 19941122 <--
WO 9201675 19920206 <--
DETD "Monocyclic aryl" means a partially or completely unsaturated carbocyclic or heterocyclic ring. Preferred monocycles include benzene, thiophene, pyridine, **furan** and pyrimidine.
DETD 4,5-bis-(4-chlorophenyl)-2-**pyrimidone**
DETD 4,5-diphenyl-2-**pyrimidone**
DETD 4,5-bis-(4-methoxyphenyl)-2-**pyrimidone**
DETD . . . such possess therapeutic value in the treatment of inflammatory conditions and hypersensitivity responses. LTB.sub.4 is implicated in diseases such as **rheumatoid arthritis**, gout, psoriasis and inflammatory bowel disease and therefore compounds which demonstrate LTB.sub.4 antagonist properties are useful in the control of. . .

L5 ANSWER 7 OF 13 USPATFULL
AN 94:44659 USPATFULL
TI Leukotriene antagonists
IN Frazee, James S., Sewell, NJ, United States
Gleason, John G., Downingtown, PA, United States
Hall, Ralph F., Villanova, PA, United States
PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 5314918 19940524 <--
AI US 1992-864156 19920402 (7)
RLI Continuation of Ser. No. US 1989-366046, filed on 14 Jun 1989, now abandoned which is a continuation-in-part of Ser. No. US 1987-66588, filed on 24 Jun 1987, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Clarke, Vera C.
LREP Kanagy, James M., Lentz, Edward T., Suter, Stuart R.
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1795
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to alkanoic acid compounds having phenyl and heteroarylthio substituents which are useful as leukotriene antagonists, processes for the preparation thereof, and pharmaceutical compositions containing such compounds.

This invention also relates to methods of treating diseases in which leukotrienes are a factor by administration of an effective amount of

the above compounds or compositions.
PI US 5314918 19940524 <--
SUMM . . . A. et al., Nature, 293, 103-108 (1981).] Leukotriene antagonists can therefore be useful in the treatment of inflammatory diseases including **rheumatoid arthritis** and gout.
SUMM M is c alkyl, ethynyl, trifluoromethyl, isopropenyl, **furanyl**, thienyl, cyclohexyl or phenyl optionally monosubstituted with Br, Cl, CF.sub.3, C.sub.1-4 alkoxy, C.sub.1-4 alkyl, methylthio, or trifluoromethylthio;
DETD M is C.sub.1-4 alkyl, ethynyl, trifluoromethyl, isopropenyl, **furanyl**, thienyl, cyclohexyl or phenyl optionally monosubstituted with Br, Cl, CF.sub.3, C.sub.1-4 alkoxy, C.sub.1-4 alkyl, methylthio, or trifluoromethylthio;
DETD . . . isolated, sensitized guinea pig trachea (a model of respiratory anaphylaxis). Exemplary of histamine H.sub.1 -receptor antagonists are mepyramine, chlorpheniramine, and 2-[4-(5-bromo-3-methylpyrid-2-yl)butylaminol-5-1(6-methyl-pyrid-3-yl)methyl]-4-**pyrimidone**, and other known H receptor antagonists.

L5 ANSWER 8 OF 13 USPATFULL
AN 92:72485 USPATFULL
TI Leukotriene antagonists containing tetrazolyl groups
IN Gleason, John G., Downingtown, PA, United States
Hall, Ralph F., Villanova, PA, United States
Uzinskas, Irene, Villanova, PA, United States
PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 5143931 19920901 <--
AI US 1990-631530 19901221 (7)
RLI Continuation of Ser. No. US 1982-66592, filed on 24 Jun 1982, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Springer, David B.
LREP Kanagy, James M., Suter, Stuart R., Lentz, Edward T.
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1520
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to alkanoic acid compounds having phenyl and heteroarylthio substituents which are useful as leukotriene antagonists and pharmaceutical compositions containing such compounds. This invention also relates to methods of treating diseases in which leukotrienes are a factor by administration of an effective amount of the above compounds or compositions.
PI US 5143931 19920901 <--
SUMM . . . A. et al., Nature, 293, 103-108 (1981).] Leukotriene antagonists can therefore be useful in the treatment of inflammatory diseases including **rheumatoid arthritis** and gout.
SUMM B is C.sub.1-4 alkyl, ethynyl, trifluoromethyl, isopropenyl, **furanyl**, thienyl, cyclohexyl or phenyl optionally monosubstituted with Br, Cl, CF.sub.3, C.sub.1-4 alkoxy, C.sub.1-4 alkyl, methylthio, or trifluoromethylthio;
SUMM W is a 5-membered heteroaryl ring selected from tetrazole, thiazole, triazole, thiophene, **furan**, oxazole, thiadiazole, pyrrole, or pyrazole, each group unsubstituted or substituted with one to three ##STR5## R.sub.4 and R.sub.5 are as. . .
DETD B is C.sub.1-4 alkyl, ethynyl, trifluoromethyl, isopropenyl, **furanyl**, thienyl, cyclohexyl, or phenyl optionally monosubstituted with Br, Cl, CF.sub.3, C.sub.1-4 alkoxy, C.sub.1-4 alkyl, methylthio, or trifluoromethylthio;

DETD W is a 5-membered ring heteroaryl group selected from tetrazole, thiazole, triazole, thiophene, **furan**, oxazole, thiadiazole, pyrrole, imidazole, or pyrazole, each group unsubstituted or substituted with one to three ##STR9## wherein R.sub.4 and R.sub.5. . .

DETD . . . H.sub.1 -receptor antagonist in amounts sufficient to inhibit antigen-induced respiratory anaphylaxis. Examples of histamine H.sub.1 -receptor antagonists include mepyramine, 2-[4-(5-bromo-3-methyl-pyrid-2yl)butylamino]-5-[(6-methyl-pyrid-3-yl) methyl]-4-**pyrimidone** and other known H.sub.1 -receptor antagonists. The above-defined dosage of a compound of formula I is conveniently employed for this. . .

CLM What is claimed is:

. . . L and T are not sulfur when q is 1 or 2; and B is C.sub.1-4 alkyl, ethynyl, trifluormethyl, isopropenyl, **furanyl**, thienyl, cyclohexyl, or phenyl optionally monsubstituted with Br, Cl, CF.sub.3, C.sub.1-4 alkyl, C.sub.1-4 alkoxy, methylthio, or thrifluoromethylthio; R.sub.2 and A. . .

L5 ANSWER 9 OF 13 USPATFULL

AN 92:63861 USPATFULL

TI Leukotriene antagonists

IN Gleason, John G., Downingtown, PA, United States
Hall, Ralph F., Villanova, PA, United States
Uzinskas, Irene, Villanova, PA, United States

PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)

PI US 5135938 19920804 <--

AI US 1990-502007 19900330 (7)

RLI Division of Ser. No. US 1987-66592, filed on 24 Jun 1987, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Gerstl, Robert

LREP Kanagy, James M., Suter, Stuart R., Lentz, Edward T.

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1481

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Leukotriene antagonist thiadiazoles have been prepared.

PI US 5135938 19920804 <--

SUMM . . . A. et al., Nature, 293, 103-108 (1981).] Leukotriene antagonists can therefore be useful in the treatment of inflammatory diseases including **rheumatoid arthritis** and gout.

SUMM B is C.sub.1-4 alkyl, ethynyl, trifluoromethyl, isopropenyl, **furanyl**, thienyl, cyclohexyl or phenyl optionally monosubstituted with Br, Cl, DF.sub.2, C.sub.1-4 alkoxy, C.sub.1-4 alkyl, methylthio, or trifluoromethylthio;

SUMM W is a 5-membered heteroaryl ring selected from tetrazole, thiazole, triazole, thiophene, **furan**, oxazole, thiadiazole, pyrrole, or pyrazole, each group unsubstituted or substituted with one to three ##STR5## R.sub.4 and R.sub.5 are as. . .

DETD W is a 5-membered ring heteroaryl group selected from tetrazole, thiazole, triazole, thiophene, **furan**, oxazole, thiadiazole, pyrrole, imidazole, or pyrazole, each group unsubstituted or substituted with one to three ##STR9## wherein R.sub.4 and R.sub.5. . .

DETD . . . H.sub.1 -receptor antagonist in amounts sufficient to inhibit antigen-induced respiratory anaphylaxis. Examples of histamine H.sub.1 -receptor antagonists include mepyramine, 2-[4-(5-bromo-3-methyl-pyrid-2-yl)butylamino]-5-[(6-methyl-pyrid-3-yl) methyl]-4-**pyrimidone** and other known H.sub.1 -receptor antagonists. The above-defined dosage of a compound of formula I is conveniently employed for this. . .

CLM What is claimed is:

. . . that L and T are not sulfur when q is 1 or 2; B is C.sub.1-4 alkyl,

ethynl, trifluoromethyl, isopropenyl, **furanyl**, thienyl, cyclohexyl, or phenyl optionally monosubstituted with Br, Cl, CF.sub.2, C.sub.1-4 alkyl, C.sub.1-4 alkoxy, methylthio, or trifluoromethylthio; R.sub.2 and A. . .

L5 ANSWER 10 OF 13 USPATFULL
AN 92:23189 USPATFULL
TI 7-deazaguanines as immunomodulators
IN Malone, Thomas C., Canton, MI, United States
Sircar, Jagadish C., Ann Arbor, MI, United States
PA Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)
PI US 5098905 19920324 <--
AI US 1990-614319 19901115 (7)
RLI Division of Ser. No. US 1990-473293, filed on 1 Feb 1990, now patented, Pat. No. US 5002950 which is a division of Ser. No. US 1989-354312, filed on 13 Mar 1989, now patented, Pat. No. US 4921858 which is a continuation of Ser. No. US 1987-86231, filed on 20 Aug 1987, now abandoned which is a continuation-in-part of Ser. No. US 1986-923521, filed on 24 Oct 1986, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Bernhardt, E.
LREP Thierstein, Joan
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 392
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is various 7-deazaguanines having activity as immunomodulators. Also included are pharmaceutical compositions and methods of use thereof.
PI US 5098905 19920324 <--
SUMM . . . carbon atoms, hydroxy, or alkoxy of from one to four carbon atoms, (ii) 2- or 3-thienyl, or (iii) 2- or 3-**furanyl** with the proviso that when R.sub.6 is OH, and R is H.sub.2 N, and R.sub.7 and R.sub.8 are both hydrogen. . .
SUMM . . . four carbon atoms, hydroxy, alkoxy of from one to four carbon atoms, (ii) 2- or 3-thienyl, or (iii) 2- or 3-**furanyl** with a pharmaceutically acceptable carrier. Thus, the invention is also a method of treating psoriasis, an autoimmune disease, such as. . .
DETD . . . SH; R.sub.2 and R.sub.8 are NH.sub.2, n is one, and Ar is 2- or 3-thienyl. A more preferred embodiment is 2-amino-7-(2-thienylmethyl)-4-pyrrolo[2,3-d)]**pyrimidone**.
DETD . . . modulation and/or removal of T-cells by thoracic duct drainage, lymphapheresis or total lymphoid irradiation gave partial to complete relief from **rheumatoid arthritis** in patients who were totally refractory to other forms of therapy (A. Tanay, et al, Arthritis and Rheumatism, Vol. 30,. . . et al, JAMA, V-256, No. 22, Dec. 12, 1986, pp. 3110-3116.) Finally, cyclosporin A is shown to be efficacious in **rheumatoid arthritis**. (M. E. Weinblatt, et al, Arthritis and Rheumatism, V-30, No. 1, pp. 11-17 (January, 1987); 0. Forre, et al, Arthritis. . .
DETD . . . to prevent rejection in transplantation or in the treatment of psoriasis and in the treatment of autoimmune disease such as **rheumatoid arthritis**, systemic lupus erythrematosus, inflammatory bowel disease, multiple sclerosis, myasthemia gravis, gout or gouty arthritis, juvenile diabetes, cancer, and viral diseases.. . .
DETD . . . and the neutralized with sodium acetate (10 g). The resulting solution was added in one portion to a mixture of 2-amino-4-(2-thienylmethyl)-6-**pyrimidone** (10 g; 45 mmol), sodium a (5.0 g)

and hot water (50 ml). The mixture was allowed to stir on. . .
DETD 2-Amino-7-(2-thienylmethyl)-4-pyrrolo[2,3-d]**pyrimidone**
CLM What is claimed:
. . . four carbon atoms, hydroxy, alkoxy of from one to four carbon atoms, (ii) 2- or 3-thienyl, or (iii) 2- or 3-**furanyl** in unit dosage form.

5. A method of claim 3 wherein the compound is 2-amino-7-(2-thienylmethyl)-4-pyrrolo[2,3-d]**pyrimidone**.

6. A method of claim 1 wherein the compound is the hydrochloride salt of 2-amino-7-(2-thienylmethyl)-4-pyrrolo[2,3-d]**pyrimidone**.

L5 ANSWER 11 OF 13 USPATFULL
AN 91:24659 USPATFULL
TI 7-deazaguanines as immunomodulators
IN Malone, Thomas C., Canton, MI, United States
Sircar, Jagadish C., Ann Arbor, MI, United States
PA Warner-Lambert CO., Morris Plains, NJ, United States (U.S. corporation)
PI US 5002950 19910326 <--
AI US 1990-473293 19900201 (7)
RLI Division of Ser. No. US 1989-354312, filed on 13 Mar 1989, now patented, Pat. No. US 4921858 which is a continuation of Ser. No. US 1987-86231, filed on 20 Aug 1987, now abandoned Continuation-in-part of Ser. No. US 1986-923521, filed on 24 Oct 1986, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Bernhardt, E.
LREP Thierstein, Joan
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 401
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is various 7-deazaguanines having activity as immunomodulators. Also included are pharmaceutical compositions and methods of use thereof.
PI US 5002950 19910326 <--
SUMM . . . carbon atoms, hydroxy, or alkoxy of from one to four carbon atoms, (ii) 2- or 3-thienyl, or (iii) 2- or 3-**furanyl** with the proviso that when R.sub.6 is OH, and R.sub.2 is H.sub.2 N, and R.sub.7 and R.sub.8 are both hydrogen. . .
SUMM . . . four carbon atoms, hydroxy, alkoxy of from one to four carbon atoms, (ii) 2- or 3-thienyl, or (iii) 2- or 3-**furanyl** with a pharmaceutically acceptable carrier. Thus, the invention is also a method of treating psoriasis, an autoimmune disease, such as. . .
SUMM . . . SH; R.sub.2 and R.sub.8 are NH.sub.2, n is one, and Ar is 2- or 3-thienyl. A more preferred embodiment is 2-amino-7-(2-thienylmethyl)-4-pyrrolo[2,3-d]**pyrimidone**.
SUMM . . . modulation and/or removal of T-cells by thoracic duct drainage, lymphapheresis or total lymphoid irradiation gave partial to complete relief from **rheumatoid arthritis** in patients who were totally refractory to other forms of therapy (A. Tanay, et al, Arthritis and Rheumatism, Vol. 30,. . . et al, JAMA, V-256, No. 22, Dec. 12, 1986, pp. 3110-3116.) Finally, cyclosporin A is shown to be efficacious in **rheumatoid arthritis**. (M. E. Weinblatt, et al, Arthitis and Rheumatism, V-30, No. 1, pp. 11-17 (January, 1987); 0. Forre, et al, Arthritis. . .
SUMM . . . to prevent rejection in transplantation or in the treatment of psoriasis and in the treatment of autoimmune disease such as **rheumatoid arthritis**, systemic lupus erythrematosus,

inflammatory bowel disease, multiple sclerosis, myasthemia gravis, gout or gouty arthritis, juvenile diabetes, cancer, and viral diseases.. .

DETD . . . and then neutralized with sodium acetate (10 g). The resulting solution was added in one portion to a mixture of 2-amino-4-(2-thienylmethyl)-6-**pyrimidone** (10 g; 45 mmol), sodium acetate (5.0 g) and hot water (50 ml). The mixture was allowed to stir on. . .

DETD 2-Amino-7-(2-thienylmethyl)-4-pyrrolo[2,3-d]**pyrimidone**

L5 ANSWER 12 OF 13 USPATFULL

AN 91:17226 USPATFULL

TI -2-Amino-4,6-dichloro-5-(2-cyanomethyl-2-amino-5(cyanomethyl)-4,6-dichloro pyrimidine

IN Malone, Thomas C., Canton, MI, United States
Sircar, Jagadish C., Ann Arbor, MI, United States

PA Warner-Lambert Company, Morris Plains, NJ, United States (non-U.S. corporation)

PI US 4996319 19910226 <--

AI US 1990-473493 19900201 (7)

RLI Division of Ser. No. US 1989-354312, filed on 13 Mar 1989, now patented, Pat. No. US 4921858 which is a continuation of Ser. No. US 1987-2727, filed on 19 Oct 1987 which is a continuation of Ser. No. US 1987-86231, filed on 20 Aug 1987, now abandoned which is a continuation-in-part of Ser. No. US 1986-923521, filed on 24 Oct 1986, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Ford, John M.

LREP Thierstein, Joan

CLMN Number of Claims: 1

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 360

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is various 7-deazaguanines having activity as immunomodulators. Also included are pharmaceutical compositions and methods of use thereof.

PI US 4996319 19910226 <--

SUMM . . . carbon atoms, hydroxy, or alkoxy of from one to four carbon atoms, (ii) 2- or 3-thienyl, or (iii) 2- or 3-**furanyl** with the proviso that when R.sub.6 is OH, and R.sub.2 is H.sub.2 N, and R.sub.7 and R.sub.8 are both hydrogen. . .

SUMM . . . four carbon atoms, hydroxy, alkoxy of from one to four carbon atoms, (ii) 2- or 3-thienyl, or (iii) 2- or 3-**furanyl** with a pharmaceutically acceptable carrier. Thus, the invention is also a method of treating psoriasis, an autoimmune disease, such as. . .

DETD . . . SH; R.sub.2 and R.sub.8 are NH.sub.2, n is one, and Ar is 2- or 3-thienyl. A more preferred embodiment is 2-amino-7-(2-thienylmethyl)-4-pyrrolo[2,3-d)]**pyrimidone**.

DETD . . . modulation and/or removal of T-cells by thoracic duct drainage, lymphapheresis or total lymphoid irradiation gave partial to complete relief from **rheumatoid arthritis** in patients who were totally refractory to other forms of therapy (A. Tanay, et al, Arthritis and Rheumatism, Vol. 30,. . . et al, JAMA, V-256, No. 22, Dec. 12, 1986, pp. 3110-3116.) Finally, cyclosporin A is shown to be efficacious in **rheumatoid arthritis**. (M. E. Weinblatt, et al, Arthritis and Rheumatism, V-30, No. 1, pp. 11-17 (Jan., 1987); O. Forre, et al, Arthritis. . .

DETD . . . to prevent rejection in transplantation or in the treatment of psoriasis and in the treatment of autoimmune disease such as **rheumatoid arthritis**, systemic lupus erythrematosus, inflammatory bowel disease, multiple sclerosis, myasthemia gravis, gout or gouty arthritis, juvenile diabetes, cancer, and viral diseases.. .

DETD . . . and then neutralized with sodium acetate (10 g). The resulting solution was added in one portion to a mixture of 2-amino-4-(2-thienylmethyl)-6-**pyrimidone** (10 g; 45 mmol), sodium acetate (5.0 g) and hot water (50 ml). The mixture was allowed to stir on. . .
DETD 2-Amino-7-(2-thienylmethyl)-4-pyrrolo[2,3-d]**pyrimidone**

L5 ANSWER 13 OF 13 USPATFULL
AN 90:34112 USPATFULL
TI 7-deazaguanines as immunomodulators
IN Malone, Thomas C., Canton, MI, United States
Sircar, Jagadish C., Ann Arbor, MI, United States
PA Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)
PI US 4921858 19900501 <--
WO 8803142 19880505 <--
AI US 1989-354312 19890313 (7)
WO 1987-US2727 19871019
19890313 PCT 371 date
19890313 PCT 102(e) date
RLI Continuation of Ser. No. US 1987-86231, filed on 20 Aug 1987, now abandoned which is a continuation-in-part of Ser. No. US 1986-923521, filed on 24 Oct 1986, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Bernhardt, E.
LREP Thierstein, Joan
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 404
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is various 7-deazaguanines having activity as immunomodulators. Also included are pharmaceutical compositions and methods of use thereof.
PI US 4921858 19900501 <--
WO 8803142 19880505 <--
SUMM . . . carbon atoms, hydroxy, or alkoxy of from one to four carbon atoms, (ii) 2- or 3-thienyl, or (iii) 2- or 3-**furanyl** with the proviso that when R.sub.6 is OH, and R.sub.2 is H.sub.2 N, and R.sub.7 and R.sub.8 are both hydrogen. . .
SUMM . . . four carbon atoms, hydroxy, alkoxy of from one to four carbon atoms, (ii) 2- or 3-thienyl, or (iii) 2- or 3-**furanyl** with a pharmaceutically acceptable carrier. Thus, the invention is also a method of treating psoriasis, an autoimmune disease, such as. . .
DETD . . . SH; R.sub.2 and R.sub.8 are NH.sub.2, n is one, and Ar is 2- or 3-thienyl. A more preferred embodiment is 2-amino-7-(2-thienylmethyl)-4-pyrrolo[2,3-d)]**pyrimidone**.
DETD . . . modulation and/or removal of T-cells by thoracic duct drainage, lymphapheresis or total lymphoid irradiation gave partial to complete relief from **rheumatoid arthritis** in patients who were totally refractory to other forms of therapy (A. Tanay, et al, Arthritis and Rheumatism, Vol. 30,. . . et al, JAMA, V-256, No. 22, Dec. 12, 1986, pp. 3110-3116.) Finally, cyclosporin A is shown to be efficacious in **rheumatoid arthritis**. (M. E. Weinblatt, et al, Arthritis and Rheumatism, V-30, No. 1, pp. 11-17 (January, 1987); O. Forre, et al, Arthritis. . .
DETD . . . to prevent rejection in transplantation or in the treatment of psoriasis and in the treatment of autoimmune disease such as **rheumatoid arthritis**, systemic lupus erythrematosus, inflammatory bowel disease, multiple sclerosis, myasthemia gravis, gout or gouty arthritis, juvenile diabetes, cancer, and viral diseases.. .

DETD . . . and then neutralized with sodium acetate (10 g). The resulting solution was added in one portion to a mixture of 2-amino-4-(2-thienylmethyl)-6-**pyrimidone** (10 g; 45 mmol), sodium acetate (5.0 g) and hot water (50 ml). The mixture was allowed to stir on. . .

DETD 2-Amino-7-(2-thienylmethyl)-4-pyrrolo[2,3-d]**pyrimidone**

CLM What is claimed is:

. . . once, n is an integer of from one through four, Ar is (i) 2- or 3-thienyl, or (ii) 2- or 3-**furanyl**; or a pharmaceutically acceptable base or acid addition salt thereof.

5. A compound of claim 3 and being 2-amino-7-(2-thienyl-methyl)-4-pyrrolo[2,3-d]**pyrimidone**.

7. A pharmaceutical composition for treating psoriasis, autoimmune diseases or rejection of transplantation comprising an antipsoriatic, antiautoimmune disease or antirejection. . . once, n is an integer of from one to four, Ar is (i) 2- or 3-thienyl, or (ii) 2- or 3-**furanyl** and a pharmaceutically acceptable carrier.